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NEWS 3 FEB 25 CA/CAPLUS - Russian Agency for Patents and Trademarks (ROSPATENT) added to list of core patent offices covered
NEWS 4 FEB 28 PATDPAFULL - New display fields provide for legal status data from INPADOC
NEWS 5 FEB 28 BABS - Current-awareness alerts (SDIs) available
NEWS 6 FEB 28 MEDLINE/LMEDLINE reloaded
NEWS 7 MAR 02 GBFULL: New full-text patent database on STN
NEWS 8 MAR 03 REGISTRY/ZREGISTRY - Sequence annotations enhanced
NEWS 9 MAR 03 MEDLINE file segment of TOXCENTER reloaded
NEWS 10 MAR 22 KOREPAT now updated monthly; patent information enhanced
NEWS 11 MAR 22 Original IDE display format returns to REGISTRY/ZREGISTRY
NEWS 12 MAR 22 PATDPASPC - New patent database available
NEWS 13 MAR 22 REGISTRY/ZREGISTRY enhanced with experimental property tags
NEWS 14 APR 04 EPFULL enhanced with additional patent information and new fields
NEWS 15 APR 04 EMBASE - Database reloaded and enhanced
NEWS 16 APR 18 New CAS Information Use Policies available online
NEWS 17 APR 25 Patent searching, including current-awareness alerts (SDIs), based on application date in CA/CAplus and USPATFULL/USPAT2 may be affected by a change in filing date for U.S. applications.
NEWS 18 APR 28 Improved searching of U.S. Patent Classifications for U.S. patent records in CA/CAplus
NEWS 19 MAY 23 GBFULL enhanced with patent drawing images
NEWS 20 MAY 23 REGISTRY has been enhanced with source information from CHEMCATS
NEWS 21 MAY 26 STN User Update to be held June 6 and June 7 at the SLA 2005 Annual Conference
NEWS 22 JUN 06 STN Patent Forums to be held in June 2005
NEWS 23 JUN 06 The Analysis Edition of STN Express with Discover! (Version 8.0 for Windows) now available

NEWS EXPRESS JANUARY 10 CURRENT WINDOWS VERSION IS V7.01a, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 10 JANUARY 2005

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STRUCTURE FILE UPDATES: 10 JUN 2005 HIGHEST RN 852098-52-3
DICTIONARY FILE UPDATES: 10 JUN 2005 HIGHEST RN 852098-52-3

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TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

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*
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
*

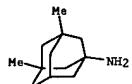
Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
<http://www.cas.org/ONLINE/DBSS/registryss.html>

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=> s (memantine hydrochloride)/cn
L1           1 (MEMANTINE HYDROCHLORIDE)/CN

=> d 11
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L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2005 ACS on STN
RN 41100-52-1 REGISTRY
ED Entered STN: 16 Nov 1984
CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA
INDEX NAME)
OTHER CA INDEX NAMES:
CN 1-Adamantanamine, 3,5-dimethyl-, hydrochloride (7CI)
OTHER NAMES:
CN 1-Amino-3,5-dimethyladamantane hydrochloride
CN 3,5-Dimethyltricyclo[3.3.1.13,7]decan-1-amine hydrochloride
CN Akatadol
CN Akura
CN Ebixia
CN Ebixa
CN from Akura
CN Memantine hydrochloride
CN Namenda
CN NSC 102290
CN SUN Y7017
MF C12 H21 N . Cl H
CI COM
LC STN Files: ADISINSIGHT, BIOPHARMA, BIOSIS, BIOTECHNO, CA, CAOLD,
CAPLUS, CASREACT, CHEMCATS, CHEMLIST, CIN, CSChem, DIOGENES, EMBASE,
IMSPATENTS, IMRRESEARCH, IPA, MEDLINE, MRCK, PATDPAASC, PHAR, PROMT,
PROSPECTOR, PS, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)
CRN (19982-08-2)



● HC1

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

46 REFERENCES IN FILE CA (1907 TO DATE)
46 REFERENCES IN FILE CAPLUS (1907 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

=> fil caplus
COST IN U.S. DOLLARS
FULL ESTIMATED COST

SINCE FILE ENTRY	TOTAL SESSION
8.16	8.37

FILE 'CAPLUS' ENTERED AT 17:42:46 ON 12 JUN 2005
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PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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FILE COVERS 1907 - 12 Jun 2005 VOL 142 ISS 25
FILE LAST UPDATED: 10 Jun 2005 (20050610/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s 41100-52-1/rn
46 41100-52-1
0 41100-52-1D
L2 46 41100-52-1/RN
(41100-52-1 (NOTL) 41100-52-1D)

=> d 12 1-46 abs ibib hitstr

L2 ANSWER 1 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN
 AB The invention is directed to formulations of pharmaceutical compds., such as the cyclohexylamines and aminoadamantanes which have antimicrobial properties. In particular, it is directed to aqueous based formulations with reduced amt. of preservatives which allow safe and convenient administration and flexible dosing and which, in the case of oral formulations, are easy to swallow. Optionally, the compds. contain compnents that provide the requisite stability and shelf life while reducing or avoiding incarceration of the composition around the container closure which leads to leakage and difficulty in opening the container. Solas were prepared containing memantine-HCl or Naramexane mesylate.

ACCESSION NUMBER: 2005-423729 CAPLUS

DOCUMENT NUMBER: 142:469279

TITLE: Antimicrobial aqueous solutions comprising cyclohexylamines and aminoadamantanes
 INVENTOR(S): Dediya, Mahendra G.; Mahashabde, Shashank; Yang, Yan; Goel, Anshu; Seiller, Erhard; Hauptmeier, Bernhard

PATENT ASSIGNEE(S): Hartz Pharma G.m.b.H. & Co. K.-G.a.A., Germany

SOURCE: PCT Int. Appl. 49 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005044228	A2	20050519	WO 2004-US37026	20041105
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LX, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AH, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG				

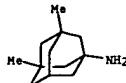
PRIORITY APPLN. INFO.: US 2003-517981P P 20031105

IT 41100-52-1, Memantine hydrochloride
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (antimicrobial aqueous solns. comprising cyclohexylamines and aminoadamantanes)

RN 41100-52-1 CAPLUS

CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)

L2 ANSWER 1 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



● HCl

L2 ANSWER 2 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN
 AB A new method of preparing memantine hydrochloride, comprises the following steps: reaction of 1-bromo-3,5-dimethyladamantane and urea/formic acid with formic acid also acting as the solvent; hydrolysis with aqueous inorg. acid; alkalization, extracting and acidifying with hydrochloric acid; finally collecting target compound. The method uses cheaper raw materials and conducts in homogeneous phase under mild conditions. It can reach high yield and good product purity, and be suitable for large scale production.

The purity of crude product is 99.0%, and reaches 99.98% after first recrystn., yield: 69.5%, bp: 332°C (DSC).

ACCESSION NUMBER: 2005-238942 CAPLUS

DOCUMENT NUMBER: 142:279886

TITLE: A method of preparing memantine hydrochloride
 INVENTOR(S): Zhang, Fulij; Hu, Meng; Zhao, Lizi; Ge, Mengya
 PATENT ASSIGNEE(S): Shanghai Institute of Pharmaceutical Industry, Peop. Rep. China; Zhejiang Kangyu Pharmaceutical Co., Ltd.

SOURCE: PCT Int. Appl., 13 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Chinese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005023753	A1	20050317	WO 2003-CN1094	20031219
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LX, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: CN 2003-150892 A 20030910

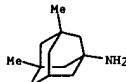
OTHER SOURCE(S): CASREACT 142:279886

IT 41100-52-1P, Memantine hydrochloride
 RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
 (preparation of memantine hydrochloride)

RN 41100-52-1 CAPLUS

CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)

L2 ANSWER 2 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



● HCl

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 3 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN
 AB The present invention provides a method of treating a cognitive dysfunction in a mammal. The method includes administering to the mammal an effective amount of a compound of choline esters (e.g., stearyl choline chloride). Comparison of donepezil hydrochloride (I) and stearyl choline chloride (II) in scopolamine impaired rats is reported. Animals treated with II also tended to learn the spatial location of the hidden platform faster and more efficiently than animals treated with I. Formulation of sustained-release pharmaceuticals containing active ingredients are also disclosed.

ACCESSION NUMBER: 2005:182612 CAPLUS

DOCUMENT NUMBER: 142-254637

TITLE: Choline esters useful for the treatment of cognitive dysfunctions and enhancement of memory, learning and cognition

INVENTOR(S): Patel, Hasmukh B.

PATENT ASSIGNEE(S): USA

SOURCE: PCT Int. Appl., 111 pp.

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005019157	A1	20050303	WO 2004-US23400	20040720
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG				
PRIORITY APPLN. INFO.:			US 2003-642455	A 20030815
			US 2003-US27062	A 20030829
			US 2004-578503P	F 20040608

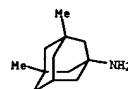
OTHER SOURCE(S): MARPAT 142:254637

IT 41100-52-1, Memantine hydrochloride

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (choline esters useful for treatment of cognitive dysfunctions and enhancement of memory, learning and cognition)

RN 41100-52-1 CAPLUS

L2 ANSWER 3 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
 CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 4 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN
 AB 1-Amino-3,5-dimethyladamtane hydrochloride, useful in medicinal practice for treatment of such diseases as Parkinson's disease, neurodegenerative disorders or glaucoma (no data), is prepared by addition of HNO₃ to a previously prepared 1,3-dimethyladamtane emulsion in HOAc at 10-30°, followed by addition of a 30-55% aqueous urea solution at mole ratios

of 1,3-dimethyladamtane to HOAc to HNO₃ to urea = 1:3-4:9-12:2.5-5.0, resp., and subsequent neutralization of the reaction mass obtained with an aqueous alkali solution, extraction and isolation of product as its hydrochloride and its crystallization from H₂O. This method provides a high-quality product

(m.p. = 324-328°, vs. >300° by prior art) that satisfies requirements of Pharmacopoeia. In an example, treating 68 mL 1,3-dimethyladamtane in 82 mL HOAc with 190 mL fuming HNO₃ at 15-20°, then after 2 h adding 140 g of a 50% solution of urea at 20-25° and holding for 1 h at 25°, heating to 110 over 2 h and holding at that temperature for 2 h, then cooling and adding 400 mL of a 30% NaOH solution at 70° and subsequent extraction into PhMe and treatment with 30 mL HCl solution gave 92% 1-amino-3,5-dimethyladamtane hydrochloride.

ACCESSION NUMBER: 2005:147670 CAPLUS

DOCUMENT NUMBER: 142:240121

TITLE: Process for preparation of 1-amino-3,5-dimethyladamtane hydrochloride from urea and 1,3-dimethyladamtane

INVENTOR(S): Klimochkin, Yu. N.; Leonova, M. V.; Timofeeva, A. K.

PATENT ASSIGNEE(S): OOO "Tsiklan", Russia; AO "Olainskii

Khimiko-Farmatsetvicheskii Zavod"

SOURCE: Russ., No pp. given

CODEN: RUXKE7

DOCUMENT TYPE: Patent

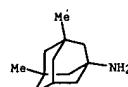
LANGUAGE: Russian

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
RU 2246492	C2	20050220	RU 2002-135270	20021225
PRIORITY APPLN. INFO.:			RU 2002-135270	20021225
OTHER SOURCE(S):	CASREACT	142:240121		
IT 41100-52-1P, 1-Amino-3,5-dimethyladamtane hydrochloride				
RL: IMP (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)				
(preparation of amino(dimethyl)adamtane hydrochloride from urea and dimethyladamtane in presence of nitric acid in acetic acid)				
RN 41100-52-1 CAPLUS				
CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)				

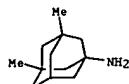
L2 ANSWER 4 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



● HCl

L2 ANSWER 5 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN
AB Compns. are provided including a neuroprotective amine related to adamantan and a polyanionic polymer which are well tolerated, non-toxic and/or result in reduced or fewer side effects. Methods are provided employing such compns., for example, topically administering such compns. to human or animal eyes, for treating human or animal eyes. Topical memantine HCl in a CMC-based formulation was tolerated up to 1.5 % w/v memantine.
ACCESSION NUMBER: 2005:122600 CAPLUS
DOCUMENT NUMBER: 142:191307
TITLE: Compositions and methods comprising memantine and polyanionic polymers for neuroprotection of eyes
INVENTOR(S): Hughes, Patrick M.; Olejnik, Orest; Schiffman, Rhett
PATENT ASSIGNEE(S): Allergan, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 14 pp., Cont.-in-part of U.S. Ser. No. 752,125.
CODEN: USXXKO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20050313652	A1	20050210	US 2004-941272	20040105
PRIORITY APPLN. INFO.:			US 2004-752125	A2 20040105
IT 41100-52-1	Memantine hydrochloride RL: BSB (Biological study, unclassified); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (memantine and polyanionic polymers for neuroprotection of eyes)			
RN 41100-52-1	CAPLUS			
CN Tricyclo[3.3.1.13.7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)				



• HCT

L2 ANSWER 7 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN
AB This invention relates to an oral dosage form containing between 1 mg and 100 mg of memantine, wherein said dosage form does not contain 10 mg of memantine or 20 mg of memantine, and wherein said dosage form is not prepared by the patient or a person administering the drug to the patient who divides the dosage form containing a larger dose of memantine. Other aspects of this invention relate to pharmaceutical products comprising the oral dosage forms and methods of administering memantine for treating glaucoma. For example, memantine-HCl 4.00% and Avicel PH101 4.00% were milled, blended with Lactose Fast F60 69.61%, Avicel PH302 16.84%, Croscarmellose sodium 5.00%, Cab-O-Sil 0.25%, and Mg stearate 0.30%, and compressed into tablets. Tablets (5 mg memantine) were then coated first with a purple coating comprising Opadry Purple 03B10434 2.00 parts and water 14.67 parts, followed by a glaze coating comprising Opadry Clear YS-1-19025-A 0.25 parts and water 4.75 parts. Tablets comprising 5 mg of memantine were administered daily to a patient suffering from glaucoma for 2 wk, followed by a tablet comprising 10 mg of memantine daily for 2 wk. At the beginning of the 4th wk of the treatment, a tablet comprising 15 mg of memantine was administered daily for as long as the drug is needed.

ACCESSION NUMBER: 2004:1082036 CAPLUS
DOCUMENT NUMBER: 142:62712
TITLE: Memantine oral dosage forms
INVENTOR(S): Firestone, Bruce A.; Vander, Zanden J.; Jacob, Terwilliger, Rodney J.; Chestham, Janet K.; Kurjan, Richard; Kuan, Teresa H.; Chang, Chin-ming; Espiritu, J. Abraham M.
PATENT ASSIGNEE(S): Allergan, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 6 pp.
CODEN: USXKCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INCOMPLIMENT:

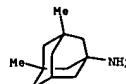
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004254251	A1	20041216	US 2004-869169	20040615
WO 2004112768	A1	20041229	WO 2004181506	20040610
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, CZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HI, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BE, GH, GM, KG, KZ, LS, MW, MN, NA, NL, SD, SZ, TZ, UG, ZW, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HI, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG				
PRIORITY APPLN. INFO.:			US 2003-478979P	P 20030616
IT 41100-52-1, Memantine hydrochloride				
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (preparation of memantine tablets for glaucoma treatment)				
RN 41100-52-1, CAPLUS				
CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEXED)				

L2 ANSWER 6 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN
 AB Memantine HCl is prepared by chlorinating 1,3-dimethyladamantane with *tert*-Bu chloride in the presence of AlCl₃ catalyst to obtain 1-chloro-3,5-dimethyladamantane, substituting with acetamide at 20-120° for 0.5-5 h to obtain 1-acetamino-3,5-dimethyladamantane, alcoholizing with ethylene glycol or glycerol in the presence of NaOH, extracting with Et₂ acetate, concentrating, salifying with HCl gas, and recrysttg. in ethanol-Et₂ acetate.

ACCESSION NUMBER: 2004:1100167 CAPLUS
 DOCUMENT NUMBER: 142:316499
 TITLE: Preparatio of memantine hydrochloride
 INVENTOR(S): Zhou, Xinqin; Xiang, Jingde; Cao, Guoxian; Hu, Mingyang; Yang, Min; Qin, Xiaofeng
 PATENT ASSIGNEE(S): Jiangsu Institute of Atomic Medicine, Peop. Rep. China
 SOURCE: Faming Zhanlan Shengqing Gongkai Shuomingshu, 7 pp.
 CODEN: CNXZEV

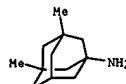
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1488622	A	20040414	CN 2003-132331	20030812
PRIORITY APPLN. INFO.:	CASREACT 142:316499 CN 2003-132331			
OTHER SOURCE(S):	IT 41100-52-1, Memantine hydrochloride			
IT	RL: IMP (Industrial manufacture); SFN (Synthetic preparation); PREP (Preparation) (Preparation of memantine hydrochloride)			
RN	41100-52-1 CAPIUS			
CN	Tricyclo[3.3.1.3,17]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CN EXACT NAME)			



● HC

L2 ANSWER 7 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



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INDEX NAME)

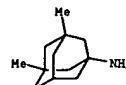
L2 ANSWER 8 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN
 AB The invention relates to a simple and improved osmotic device for the controlled release of an active agent from the core into the use environment. According to the invention, the active agent is first released through a preformed passage and, subsequently, through a second passage which is formed in situ. Optionally, the size of one or both of the passages increases during the use of the osmotic device. Moreover, the preformed passage and/or the second passage increases the release speed of the active agent and enables the release of active agents which are essentially insol. in the use environment. Owing to the in situ formation of the second opening, the device can release a greater percentage of active agent than that which would be released without said second opening.

ACCESSION NUMBER: 2004:1036887 CAPLUS
 DOCUMENT NUMBER: 142:11520
 TITLE: Breakable, controlled-release tablets comprising a preformed passage
 INVENTOR(S): Fasur, Joaquin/vergez, Juan A.
 PATENT ASSIGNEE(S): Osmotic Costa Rica, Sociedad Anonima, Costa Rica
 SOURCE: PCT Int. Appl., 65 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: Spanish
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004103349	A2	20041202	WO 2004-CR5	20040521
WO 2004103349	A3	20050331		
W:	AZ, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, VA, UG, US, UZ, VC, VN, YU, ZA, ZH, ZW			
RW:	BW, GH, KE, LS, MW, MZ, NA, SD, SE, SZ, TZ, UG, ZH, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

US 2005008702 A1 20050113 US 2004-851866 20040521
 PRIORITY APPLN. INFO.: US 2003-472819P P 20030522
 IT 41100-52-1, Memantine hydrochloride
 RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (breakable, controlled-release tablets comprising a preformed passage)
 RN 41100-52-1 CAPLUS
 CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)

L2 ANSWER 8 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

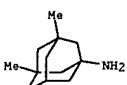


● HCl

L2 ANSWER 9 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN
 AB A review. Memantine (Axura, Merz Pharmaceuticals GmbH; Ebixa, H. Lundbeck A/S, Namenda, Forest Labs., Inc.) is an uncompetitive N-methyl-D-aspartate (NMDA) receptor antagonist with low to moderate affinity for the (+)MK-801 binding site. It is characterized as a voltage-sensitive open-channel NMDA receptor blocker that antagonizes NMDA receptor-mediated inward currents in vitro with an IC50 of 1-3 μ M. In animal models, memantine displays both neuroprotective (antieexcitotoxic) and cognition-enhancing properties at therapeutically relevant concns. The strong voltage dependency and rapid blocking/unblocking kinetics of memantine are thought to be the basis for its excellent clin. tolerability. Recently completed clin. studies demonstrate pos. effects of memantine in Alzheimer's disease both as a monotherapy and in patients receiving continuous donepezil treatment. Memantine treatment also has demonstrated significant improvement of cognitive performance in patients suffering from vascular dementia. Furthermore, the safety and tolerability of memantine in clin. trials has been excellent, with the incidence of premature withdrawals due to adverse events no greater than placebo and overall low frequencies of total adverse events. In 2002, memantine was approved by the European Medicines Agency (EMEA) for the treatment of moderately severe to severe Alzheimer's disease. More recently, memantine was approved in the US for the treatment of moderate to severe Alzheimer's disease (Oct. 2003). Here, we review the most recent pharmacol. and clin. data in dementia patients that has emerged from the systematic evaluation of memantine.

ACCESSION NUMBER: 2004:909501 CAPLUS
 DOCUMENT NUMBER: 142:189916
 TITLE: Memantine hydrochloride: pharmacological and clinical profile
 AUTHOR(S): Moebius, Hans J.; Stoeffler, Albrecht; Graham, Stephen M.
 CORPORATE SOURCE: Merz Pharmaceuticals, Frankfurt, Germany
 SOURCE: Drugs of Today (2004), 40(8), 685-695
 CODEN: MDACAP; ISSN: 0025-7656
 PUBLISHER: Frouz Science
 DOCUMENT TYPE: Journal; General Review
 LANGUAGE: English
 IT 41100-52-1, Axura
 RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (Namenda, Ebixa; memantine hydrochloride pharmcol. and clin. profile)
 RN 41100-52-1 CAPLUS
 CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)

L2 ANSWER 9 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

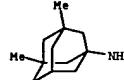


● HCl

L2 ANSWER 10 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN
 AB Objective: The aim of the present study was to predict the drug interaction potential of memantine by elucidation of its inhibitory effects on Cytochrome P 450 enzymes using pooled human liver microsomes (HLM) and recombinant P450s. Methods: The inhibitory potency of memantine on CYP1A2, CYP2A6, CYP2B6, CYP2C9, CYP2C19, CYP2D6, CYP2E1, and CYP3A4 activities was examined with specific probe drugs in HLM and recombinant P450s. In the *in vivo* drug interactions of memantine were predicted *in vitro* using the $[I]/([I] + K_i)$ values. Results: In HLM, memantine inhibited CYP2B6 and CYP2D6 activities, with K_i (I_{50}) values of 76.7 (279.7) and 94.9 (369.7) μM , resp. Both inhibitions were competitive. In addition, cDNA-expressed P450s were used to confirm these results. Memantine strongly inhibited recombinant CYP2B6 activity with I_{50} (K_i) value of 1.12 (0.51) μM and activity of recombinant CYP2D6 with I_{50} (K_i) value of 242.4 (84.4) μM . With concns. up to 1,000 μM , memantine showed no appreciable effect on CYP1A2, CYP2C9, or CYP3A4 activities and a slight decrease of CYP2A6 and CYP2C19 activities. Based on $[I]/([I] + K_i)$ values calculated using peak total plasma concentration (or enzyme-available concentration in the liver) of memantine and the K_i obtained in HLM, 1.3 (13.5), and 1.0 (11.2), inhibition of the clearance of CYP2B6 and CYP2D6 substrates could be expected, resp. Nevertheless, when considering K_i values obtained from cDNA-expressed CYP2B6, as generally recommended, even 66.2 (95.9) decrease in metabolism of coadministered CYP2B6 substrates could be anticipated. Conclusion: Memantine exerts selective inhibition of CYP2B6 activity at clin. relevant concns., suggesting the potential for clin. significant drug interactions. Inhibition of other CYPs during memantine therapy is unlikely. Moreover, memantine represents a new, potent, selective inhibitor of recombinant CYP2B6, which may prove useful for screening purposes during early phases of *in vitro* drug metabolism studies.

with new chemical entities.
 ACCESSION NUMBER: 2004:870590 CAPLUS
 DOCUMENT NUMBER: 142:190169
 TITLE: Inhibitory effects of memantine on human cytochrome P450 activities: prediction of *in vivo* drug interactions
 AUTHOR(S): Micuda, Stanislav; Mundlova, Lucie; Anzenbacherova, Eva; Anzenbacher, Pavel; Chladek, Jaroslav; Fuksa, Leos; Martinkova, Jirina
 CORPORATE SOURCE: Department of Pharmacology, Medical Faculty of Charles University, Hradec Kralove, 500 38, Czech Rep.
 SOURCE: European Journal of Clinical Pharmacology (2004), 60(8), 583-589
 CODEN: EUCPAS; ISSN: 0031-6970
 PUBLISHER: Springer GmbH
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 IT 41100-52-1, Memantine hydrochloride
 RL: PKT (Pharmacokinetics); BIOL (Biological study)
 (noncompetitive NMDA antagonist memantine exerted inhibitory effect on CYP2B6 with weak or no influence on metabolic activities of CYP1A2, CYP2A6, CYP2C9, CYP2C19, CYP2D6, CYP2E1 and CYP3A4 using human liver microsomes and recombinant P 450)
 RN 41100-52-1 CAPLUS
 CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA
 INDEX NAME)

L2 ANSWER 10 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



● HCl
 REFERENCE COUNT: 46

THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

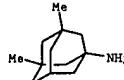
L2 ANSWER 11 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN
 AB The inotropic Glu receptors N-methyl-D-aspartate (NMDA) and α -amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptors are present peripherally in the primary sensory afferent neurons innervating the viscera. Multiple studies have reported roles of Glu receptors in gastric functions. However, no study has previously shown the direct influence of inotropic Glu receptor antagonist on vagal sensory neurons. The objective of this study was to investigate the effects of NMDA and AMPA receptor antagonists on mechanotransduction properties of vagal afferent fibers innervating the rat stomach. Action potentials were recorded from the hypnodal vagus nerve innervating the antrum of the Long-Evans rats. For antral distension (AD), a small latex balloon was inserted into the stomach and positioned in the antrum. The antral contractions were recorded with solid-state probe inserted into the water-filled balloon. Antral units were identified to isovolumic (0.2-1 ml) or isobaric AD (5-60 mm Hg). NMDA and AMPA receptor antagonists were injected in a cumulative fashion (1-100 $\mu\text{mol}/\text{kg}$, i.v.). After the conclusion of experiment, the abdomen was opened and receptive field was mapped.

by probing the serosa of the stomach. Thirty-two fibers were identified to AD. The receptive fields of 26 fibers were located in the posterior part of the antrum. All fibers exhibited spontaneous firing (mean: 7.0 impulses/s). Twenty fibers exhibited a rhythmic firing that was in phase with antral contractions, whereas 12 fibers exhibited non-rhythmic spontaneous firing unrelated to spontaneous antral contraction. Both groups of fibers exhibited a linear increase in responses to graded isovolumic or isobaric distensions. NMDA (memantine HCl and dizocilpine (MK-801)) and AMPA/kainate (6-cyano-7-nitroquinoxaline 2,3-dione; CNQX) receptor antagonists dose-dependently attenuated the mechanotransduction properties of these fibers to AD. However, competitive NMDA antagonist DL-2-amino-5 phosphonopentanoic acid (AP-5) had no effect. The study documents that Glu receptor antagonists can attenuate responses of gastric vagal sensory afferent fibers innervating the distal stomach, offering insight to potential pharmacol. agents in the treatment of gastric disorders.

ACCESSION NUMBER: 2004:322482 CAPLUS
 DOCUMENT NUMBER: 140:417661
 TITLE: Response properties of antral mechanosensitive afferent fibers and effects of ionotropic glutamate receptor antagonists
 AUTHOR(S): Sengupta, J. N.; Petersen, J.; Peles, S.; Shaker, R.
 CORPORATE SOURCE: MaccFund Research Center, Division of Gastroenterology and Hepatology, Medical College of Wisconsin, Milwaukee, WI, 53226, USA
 SOURCE: Neuroscience (Oxford, United Kingdom) (2004), 125(3), 711-723
 CODEN: NRSCDN; ISSN: 0306-4522
 PUBLISHER: Elsevier Science Ltd.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 IT 41100-52-1, Memantine hydrochloride
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (response properties of antral mechanosensitive afferent fibers and effects of inotropic Glu receptor antagonists)

RN 41100-52-1 CAPLUS
 CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA
 INDEX NAME)

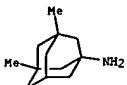
L2 ANSWER 11 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



● HCl
 REFERENCE COUNT: 57

THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

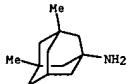
L2 ANSWER 12 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN
 AB Memantine HCl was synthesized from 1,3-dimethyladamantane by bromination, acetylation with acetonitrile in H2SO4, and hydrolysis with an overall yield of 67.8%.
 ACCESSION NUMBER: 2003:1011883 CAPLUS
 DOCUMENT NUMBER: 141:53977
 TITLE: Synthesis of memantine hydrochloride
 AUTHOR(S): Zou, Yong; Xiong, Xiaoyun; Mai, Qibing
 CORPORATE SOURCE: Guangzhou Institute of Chemistry, Chinese Academy of Sciences, Guangzhou, 510650, Peop. Rep. China
 SOURCE: Zhongguo Yiyao Gongye Zaishi (2003), 34(5), 213-214
 CODEN: ZYGEZA; ISSN: 1001-8255
 PUBLISHER: Zhongguo Yiyao Gongye Zaishi Bianjibu
 DOCUMENT TYPE: Journal
 LANGUAGE: Chinese
 OTHER SOURCE(S): CASREACT 141:53977
 IT 41100-52-1P, Memantine hydrochloride
 RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (synthesis of memantine hydrochloride)
 RN 41100-52-1 CAPLUS
 CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

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L2 ANSWER 13 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



● HCl

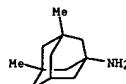
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 13 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN
 AB The objectives of this study were to characterize sepiu, synthetic, and bovine melanin and to determine their binding characteristics to the drug memantine. Phys. methods were used to characterize sepiu, synthetic, and bovine melanin. Their binding properties toward memantine were determined in deionized water and phosphate-buffered saline (PBS) at 37°. Melanin-memantine binding was measured indirectly by determining the unbound fraction of memantine. Curve fitting according to the Langmuir binding isotherm for one binding site was used for the determination of binding capacity (Bmax) and dissociation constant (KD). Synthetic and sepiu melanin had comparable Gaussian particle size distributions, whereas bovine melanin showed a heterogeneous distribution profile. The suspension medium had a small effect on the particle size distribution of synthetic and bovine melanin. There were characteristic differences in the IR spectra of the melanins. The rank order for Bmax in deionized water was sepiu > bovine > synthetic melanin. However, when the melanins were suspended in PBS, the Bmax values were lower, and the rank order was bovine > sepiu > synthetic. Whereas the KD values for sepiu and synthetic melanin remained largely the same in deionized water and PBS, the KD value for bovine melanin in PBS was more than twice than in deionized water. This study showed that the phys. characteristics of the melanins investigated differ markedly. The binding of memantine to melanin is thought to be determined by the different chemistries of the melanins, particle size, and buffer electrolytes.
 ACCESSION NUMBER: 2003:814624 CAPLUS
 DOCUMENT NUMBER: 140:292422
 TITLE: Binding of Memantine to Melanin: Influence of Type of Melanin and Characteristics
 AUTHOR(S): Koebere, Martin J.; Hughes, Patrick M.; Skellern, Graham G.; Wilson, Clive G.
 CORPORATE SOURCE: Strathclyde Institute for Biomedical Sciences, Department of Pharmaceutical Sciences, University of Strathclyde, Glasgow, UK
 SOURCE: Pharmaceutical Research (2003), 20(10), 1702-1709
 CODEN: PHAREB; ISSN: 0742-8741
 PUBLISHER: Kluwer Academic/Plenum Publishers
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 IT 41100-52-1, Memantine hydrochloride
 RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (binding of memantine to melanin)
 RN 41100-52-1 CAPLUS
 CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)

L2 ANSWER 14 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN
 AB This invention pertains to a method for producing memantine-HCl by reacting 1-bromo-3,5-dimethyladamantane with urea in a polyol solvent (such as HOCH2CH2OH), followed by treatment with NaOH, and acidification with hydrochloric acid (70-78%). The title compound can be used as an N-methyl-D-aspartic acid (NMDA) receptor antagonist for curing dementia (no data). This method features safe and simple operation and low cost.

ACCESSION NUMBER: 2003:626610 CAPLUS
 DOCUMENT NUMBER: 139:133274
 TITLE: Process for preparation of memantine hydrochloride
 INVENTOR(S): Zou, Yong; Zhu, Jie; Xiong, Xiaoyun
 PATENT ASSIGNEE(S): Guangzhou Inst. of Chemistry, Chinese Academy of Sciences, Peop. Rep. China
 SOURCE: Faming Zhanlu Shengqing Gongkai Shuomingshu, 5 pp.
 CODEN: CNXKEV
 DOCUMENT TYPE: Patent
 LANGUAGE: Chinese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1400205	A	20030305	CN 2002-134628	20020830
PRIORITY APPLN. INFO.: CN 2002-134628				
OTHER SOURCE(S):	CASREACT 139:133274			
IT 41100-52-1P, Memantine hydrochloride	RL: SPN (Synthetic preparation); PREP (Preparation) (process for preparation of memantine hydrochloride)			
RN 41100-52-1 CAPLUS	CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)			



● HCl

L2 ANSWER 15 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN
 AB Pharmaceutical conjugates are disclosed which have a therapeutic component and an efficacy-enhancing component that enhances the pharmacokinetic disposition of the therapeutic component. In one embodiment, the therapeutic component is joined to an efficacy-enhancing component by a linker. In one embodiment, the therapeutic component and the efficacy-enhancing component disassoc. under physiol. conditions, preferably near the site where the therapeutic component may exert a therapeutic effect. The efficacy-enhancing component is an adamantane derivative, e.g. a memantine.

ACCESSION NUMBER: 2003:473262 CAPLUS

DOCUMENT NUMBER: 139:30756

TITLE: Adamantane derivative-containing pharmaceutical conjugates with enhanced pharmacokinetic characteristics

INVENTOR(S): Hughes, Patrick M.; Olejnik, Orest
 PATENT ASSIGNEE(S): Allergan Sales, Inc., USA
 SOURCE: U.S. Pat. Appl. Publ., 11 pp.

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003114460	A1	20030619	US 2001-16850	20011214
CA 2471589	AA	20030626	CA 2002-2471589	20021213
WO 2003051400	A1	20030626	WO 2002-US40153	20021213
W: AB, AG, AL, AM, AT, AU, AZ, BA, BE, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GR, HN, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TH, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, EG, KZ, MD, RU, TJ, TM, AL, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BE, BJ, CF, CG, CI, CH, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1455837	A1	20040915	EP 2002-79584	20021213
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, HK, CY, AL, TR, BG, CZ, EE, SK				
JP 2005516017	Y2	20050602	JP 2003-552332	20021213
PRIORITY APPLN. INFO.:			US 2001-16850	A 20011214
			WO 2002-US40153	W 20021213

OTHER SOURCE(S): MARPAT 139:30756

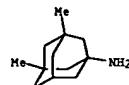
IT 41100-52-1, Memantine hydrochloride

RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (adamantane derivative-containing pharmaceutical conjugates with enhanced pharmacokinetic characteristics)

RN 41100-52-1 CAPLUS

CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)

L2 ANSWER 15 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



● HC1

L2 ANSWER 16 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN

AB Alzheimer's disease (AD) is a devastating illness that causes enormous emotional stress to affected families and is associated with substantial medical and nonmedical costs. To determine the effects of 28 wk of memantine

treatment for patients with AD on resource utilization and costs, a multicenter, prospective, double-blind, randomized, placebo-controlled clin. trial was performed in the US. The Wilcoxon-Mann-Whitney test was used to examine the resource utilization variables and logistic regression models were used for multivariate resource utilization analyses. Anal. of covariance (ANCOVA) models (log and non-log) were computed to examine costs from a societal perspective. All costs were calculated in 1999 US dollars. Outpatients with moderate to severe AD were studied. Overall, 252 patients received randomized treatment, and 166 patients (placebo n = 76, memantine n = 90) formed the treated-per-protocol (TPP) subset for the health economic analyses, on which the main cost anal. was based. The main outcome measure was the Resource Utilization in Dementia (RUD) scale, measuring patient and caregiver resource utilization, and various sources for cost calcns. Controlling for baseline differences between the groups, significantly less caregiver time was needed for patients receiving memantine than for those receiving placebo (difference 51.5 hr mo; 95% CI -95.27, -7.17; p = 0.02). Anal. of residential status also favored memantine: time to institutionalization (p = 0.052) and institutionalization at week 28 (p = 0.04 with the chi-square test). Total costs from a societal perspective were lower in the memantine group (difference \$US1089.74/mo [non-overlapping 95% CI for treatment difference -1954.90, -224.58]; p = 0.01). The main differences between the groups were total caregiver costs (\$US-823.77/mo; p = 0.03) and direct nonmedical costs (\$US-430.84/mo; p = 0.07) favoring memantine treatment. Patient direct medical costs were higher in the memantine group (p < 0.01) mainly due to the cost of memantine. Resource utilization and total health costs were lower in the memantine group than the placebo group. The results suggest that memantine treatment of patients with moderate to severe AD is cost saving from a societal perspective.

ACCESSION NUMBER: 2003:341302 CAPLUS

DOCUMENT NUMBER: 139:79012

TITLE: Resource utilisation and cost analysis of memantine in patients with moderate to severe Alzheimer's disease

AUTHOR(S): Wimo, Anders; Winblad, Bengt; Stoessl, Albrecht; Wirth, Yvonne; Moebius, Hans-Joerg

CORPORATE SOURCE: Division of Geriatric Epidemiology (Sector of Health Economy), Neurotec, Karolinska Institute, Huddinge, Sweden

SOURCE: *PharmacoEconomics* (2003), 21(5), 327-340

CODEN: PARMEK; ISSN: 1170-7690

PUBLISHER: Adis International Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

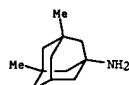
IT 41100-52-1, Memantine hydrochloride

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (resource utilization and cost anal. of memantine in patients with moderate to severe alzheimer's disease)

RN 41100-52-1 CAPLUS

CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)

L2 ANSWER 16 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

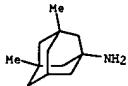


● HC1

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 17 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN
 AB The process comprises acetylaminating 1-bromo-3,5-dimethyladamantane with acetonitrile in the presence of H2SO4, pouring into ice/water, precipitating at 0-5° for 10-14 h to obtain 1-acetylaminoo-3,5-dimethyladamantane; treating with polyol (such as 1,2-ethanediol) in the presence of NaOH, extracting with chloroform, concentrating, acidifying with HCl, and recryst. in chloroform.
 ACESSION NUMBER: 2003:238375 CAPLUS
 DOCUMENT NUMBER: 138:221260
 TITLE: Synthesis of memantine hydrochloride
 INVENTOR(S): Zou, Yong; Xiong, Xiaoyun; Wei, Wen
 PATENT/ASSIGNEE(S): Guangzhou Inst. of Chemistry, Academia Sinica, Peop. Rep. China
 SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 5 pp.
 CODEN: CNOKEV
 DOCUMENT TYPE: Patent
 LANGUAGE: Chinese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

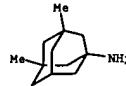
PATENT NO. KIND DATE APPLICATION NO. DATE
 CN 1335209 A 20020213 CN 2001-127788 20010829
 CN 1125033 B 20031022
 PRIORITY APPLN. INFO.: CASREACT 138:221260
 OTHER SOURCE(S): IT 41100-52-1P, Memantine hydrochloride
 RL: IMP (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
 (synthesis of memantine hydrochloride)
 RN 41100-52-1 CAPLUS
 CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

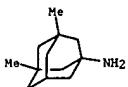
L2 ANSWER 18 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN
 AB 5-Amino-1,3-dimethyltricyclo[3.3.1.13,7]decan hydrochloride is prepared in high yield and selectivity by the amination of 5-chloro-1,3-dimethyltricyclo[3.3.1.13,7]decan with formamide, followed by extraction of the intermediate with toluene and saponification with aqueous hydrochloric acid.
 ACESSION NUMBER: 2002:644318 CAPLUS
 DOCUMENT NUMBER: 137:140294
 TITLE: Amination process for preparing the hydrochloride of 5-amino-1,3-dimethyltricyclo[3.3.1.13,7]decan from 5-chloro-1,3-dimethyltricyclo[3.3.1.13,7]decan and formamide
 INVENTOR(S): Kysilka, Vladimir; Zizkova, Vera; Bystra, Dagmar; Palasova, Lenka
 PATENT/ASSIGNEE(S): Lachema, A. S., Czech Rep.
 SOURCE: Czech Rep., 4 pp.
 CODEN: CZXKD
 DOCUMENT TYPE: Patent
 LANGUAGE: Czech
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE
 CZ 208445 B6 20010613 CZ 1996-1813 19960620
 PRIORITY APPLN. INFO.: CZ 1996-1813 19960620
 OTHER SOURCE(S): IT 41100-52-1P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (amination process for preparing the hydrochloride of 5-amino-1,3-dimethyltricyclo[3.3.1.13,7]decan from 5-chloro-1,3-dimethyltricyclo[3.3.1.13,7]decan and formamide)
 RN 41100-52-1 CAPLUS
 CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

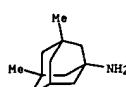
L2 ANSWER 19 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN
 AB A review, discussing the action mechanism and pharmacol. of memantine hydrochloride, a new possible agent for Alzheimer's disease.
 ACESSION NUMBER: 2002:604203 CAPLUS
 DOCUMENT NUMBER: 138:147016
 TITLE: Memantine hydrochloride, a new possible agent for Alzheimer's disease
 AUTHOR(S): Kihara, Tetsuroh
 CORPORATE SOURCE: Pharmaceutical Div., Project Planning Development, Suntory Limited, Japan
 SOURCE: BIO Clinica (2002), 17(9), 802-805
 CODEN: BCILCY; ISSN: 0919-8237
 PUBLISHER: Hokuryukan
 DOCUMENT TYPE: Journal; General Review
 LANGUAGE: Japanese
 IT 41100-52-1, Memantine hydrochloride
 RL: DMA (Drug mechanism of action); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (memantine hydrochloride, a new possible agent for Alzheimer's disease)
 RN 41100-52-1 CAPLUS
 CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

L2 ANSWER 20 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN
 AB A review. Memantine hydrochloride, an NMDA antagonist, was launched in Germany by Merz in 1989 for the treatment of dementia, an indication for which development was continuing in other markets. It is also under development by Merz, Lundbeck, Neurobiol. Technologies Inc (NTI), Forest Labs, and Suntory for the potential treatment of Alzheimer's disease (AD), AIDS-related dementia and pain in patients with neuropathy, and by Allergan for the potential treatment of ocular disease. By July 2001, a regulatory filing for neuropathic pain was expected in 2003. In Feb. 2002, the CPMP recommended to the EU commission to approve memantine for the treatment of moderately-severe to severe Alzheimer's disease. At this time, marketing authorization was expected late in the first half of 2002, and Lundbeck planned to launch memantine under the brand name Ebixa during the second half of 2002. Merz and Lundbeck, filed memantine for AD in the EU in Sept. 2000 and a NDA was submitted in Nov. of that year. The compound was in phase II trials in the US for the treatment of AIDS-related dementia and pain by August 1996 and phase III trials for glaucoma and neuroprotection by 1999. Analysts at Merrill Lynch predicted in Oct. 2001 that Allergan would make regulatory filings in the US for memantine in glaucoma and ocular hypertension in 2005, and that Forest Labs. would file for memantine in the US as a supplement to Alzheimer's disease data in early 2002, and for the treatment of neuropathic pain in 2003. Sales of \$25 million in 2004, rising to \$75 million in 2005, were predicted by Merrill Lynch for this product (429181).

ACCESSION NUMBER: 2002:580307 CAPLUS
 DOCUMENT NUMBER: 137:149666
 TITLE: Memantine (Merz)
 AUTHOR(S): Kilpatrick, Gavin J.; Tilbrook, Gary S.
 CORPORATE SOURCE: CeNeS Ltd, Cambridge, CB4 9ZR, UK
 SOURCE: Current Opinion in Investigational Drugs (PharmaPress Ltd.) (2002), 3(5), 798-806
 CODEN: COIDAZ; ISSN: 1472-4472
 PUBLISHER: PharmaPress Ltd.
 DOCUMENT TYPE: Journal; General Review
 LANGUAGE: English
 IT 41100-52-1, SUN Y017
 RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (memantine for Alzheimer disease, AIDS dementia complex, neuropathy and ocular disease)
 RN 41100-52-1 CAPLUS
 CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)



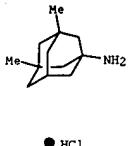
● HCl

REFERENCE COUNT: 79 THERE ARE 79 CITED REFERENCES AVAILABLE FOR THIS

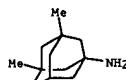
L2 ANSWER 21 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN
AB The invention relates to the use of substances for the manufacturing of a pharmaceutical composition or medicament for the treatment of disturbances or illnesses which are linked to malfunction of an ionotropic acetylcholine receptor and/or a calcium-activated potassium channel functionally associated with said acetylcholine receptor, wherein said substance is at least one adamantane derivative
ACCESSION NUMBER: 2002:240554 CAPLUS
DOCUMENT NUMBER: 136:257271
TITLE: Treatment of diseases such as leukemia and deafness with adamantane derivatives
INVENTOR(S): Ruppertsberg, J. Peter; Fakler, Bernd
PATENT ASSIGNEE(S): Tinnitis Forschungs-Und Entwicklungs G.m.b.H., Germany
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXX02
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002024187	A2	20020328	WO 2001-EP10927	20010921
WO 2002024187	A3	20030522		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KE, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MN, NE, TD, TG				
EP 1190713	A1	20020327	EP 2000-120660	20000921
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
EP 1201234	A2	20020502	EP 2000-121508	20000929
EP 1201234	A3	20030312		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
CA 2422535	AA	20020328	CA 2001-2422535	20010921
AU 2001089903	A5	20020402	AU 2001-09903	20010921
EP 1335822	A2	20030813	EP 2001-969751	20010921
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2004048892	A1	20040311	US 2003-380845	20030730
PRIORITY APPLN. INFO.:			EP 2000-120660	A 20000921
			EP 2000-121508	A 20000929
			WO 2001-EP10927	W 20010921

OTHER SOURCE(S): MRPAT 136:257271
IT 41100-52-1
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of diseases such as leukemia and deafness with adamantane derivs.)
RN 41100-52-1 CAPLUS
CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)



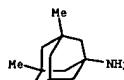
L2 ANSWER 22 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN
AB The stability consts. for the inclusion complexes of β -cyclodextrin (β -CD) with various adamantane derivs. (ADA), namely the amantanidinium (AM), rimantadinium (RIM), and memantinium (MEM) cations have been determined by UV-Vis spectrophotometry. All expts. have been performed at a pH of 1.7 and 25 °C on aqueous solns. adjusted to an ionic strength of 0.05 M (Na, H⁺)ClO₄. The competitive binding method has been used whereby methyl orange (MO) is first encapsulated by β -CD and is then substituted by ADA. It has been shown that the derivs. studied form host-guest type complexes. The calculated stability consts., reported as log K₁, were estimated to be 3.9 ± 0.1, 5.1 ± 0.2 and 3.3 ± 0.1, for AM, RIM and MEM, resp. The factors that govern the strength of binding ADA with β -CD have been discussed and an attempt was made to rationalize the variation in the established stability consts. for the ADA- β -CD complexes. General exptl. conditions required for the determination of the stability consts. of ADA with β -CD with the use of MO as an auxiliary agent were evaluated. The optimized exptl. conditions are recommended. It has been concluded that MO, even though commonly used in this type of study, does not meet the optimal and recommended conditions.
ACCESSION NUMBER: 2001:736068 CAPLUS
DOCUMENT NUMBER: 135:294641
TITLE: Stability constants of the inclusion complexes of β -cyclodextrin with various adamantane derivatives. A UV-Vis study
AUTHOR(S): Vashi, Preeti R.; Cukrowski, Ignacy; Havel, Josef
CORPORATE SOURCE: School of Chemistry, Univ. of the Witwatersrand, Johannesburg, 2050, S. Afr.
SOURCE: South African Journal of Chemistry [online computer file] (2001), 54, 1-18
CODEN: SAJCDG ISSN: 0379-4350
URL: http://ejour.sabinet.co.za/images/ejour/chem/chem_v54_a5.pdf?sessionid=01-62329-1648007521
PUBLISHER: South African Chemical Institute
DOCUMENT TYPE: Journal; [online computer file]
LANGUAGE: English
IT 41100-52-1, Memantine hydrochloride
RL: PEP (Physical, engineering or chemical process); PRP (Properties);
PROC (Process)
(adamantyl ammonium encapsulation with β -cyclodextrin after methyl orange displacement)
RN 41100-52-1 CAPLUS
CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)



L2 ANSWER 22 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
 REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 23 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
 AB A combined antidotal treatment with Memantine-HCl (MEM, 18 mg/kg, s.c.) and atropine sulfate (ATS, 16 mg/kg, s.c.) provided complete protection against acute carbofuran toxicity (1.5 mg/kg, s.c.) in rats by multiple mechanisms. Carbofuran, in addition to inhibiting serine-containing esterases, also perturbed the activities of mitochondrial/cytoplasmic biomarker enzymes (creatinine kinase, CK, and lactic dehydrogenase, LDH) in diaphragm muscle. The observed changes in the activity of biomarker enzymes were reflected in serum as a result of their leakage from the diaphragm due to a depletion of high-energy phosphates, such as ATP (274) and phosphocreatine (PC, 331), and their metabolites (ADP, 361; AMP, 358; and Cr, 381). Combined treatment with MEM and ATS provided protection and reversal of the induced changes in biomarkers by preventing the depletion of the high-energy phosphates and thus maintaining normal cell membrane characteristics, including permeability and integrity. These results, along with those reported previously, indicate that MEM antagonizes carbofuran toxicity by multiple mechanisms.

ACCESSION NUMBER: 2000:194628 CAPLUS
 DOCUMENT NUMBER: 133:54712
 TITLE: Role of high-energy phosphates and their metabolites in protection of carbofuran-induced biochemical changes in diaphragm muscle by Memantine
 AUTHOR(S): Gupta, Ramesh C.; Goad, John T.
 CORPORATE SOURCE: Toxicology Department, Breathitt Veterinary Center, Murray State University, Hopkinsville, KY, 42241-2000, USA
 SOURCE: Archives of Toxicology (2000), 74(1), 13-20
 PUBLISHER: Springer-Verlag
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 IT 41100-52-1, Memantine hydrochloride
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
 (role of high-energy phosphates and their metabolites in protection of carbofuran-induced biochemical changes in diaphragm muscle by Memantine)
 RN 41100-52-1 CAPLUS
 CN Tricyclo[3.3.1.13.7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

REFERENCE COUNT: 59 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

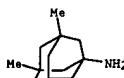
L2 ANSWER 24 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
 AB Pharmaceutical compds. having NMDA antagonist activity are used for treating certain conditions in the gastrointestinal tract, such as functional gastrointestinal disorders, and in particular irritable bowel syndrome (IBS). Also provided are pharmaceutical compns. for the treatment of IBS and a product comprising such compds. and a pharmaceutically acceptable carrier.

ACCESSION NUMBER: 1999:708596 CAPLUS
 DOCUMENT NUMBER: 131:317787
 TITLE: Use of NMDA antagonists for treatment of gastrointestinal disorders including irritable bowel syndrome
 INVENTOR(S): Asghar, Aziz; Cabero, Jose Luis; Dray, Andrew; King, Anne
 PATENT ASSIGNEE(S): Astra Aktiebolag, Swed.
 SOURCE: PCT Int. Appl., 24 pp.
 CODEN: PIKXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9955323	A1	19991104	WO 1999-SE702	19990428
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2329328	AA	19991104	CA 1999-2329328	19990428
AU 9943024	A1	19991116	AU 1999-43024	19990428
AU 760783	B2	20030522		
BR 9909971	A	20001226	BR 1999-9971	19990428
EP 1073431	A1	20010207	EP 1999-947024	19990428
EP 1073431	B1	20040707		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002512956	T2	20020508	JP 2000-545522	19990428
NZ 507436	A	20030926	NZ 1999-507436	19990428
AT 270545	E	20040715	AT 1999-947024	19990428
ES 2221753	T3	20050101	ES 1999-947024	19990428
TW 570793	B	20040111	TW 1999-88113888	19990813
NO 2000005386	A	20001026	NO 2000-5386	20001026
HK 1033876	A1	20050304	HK 2001-104450	20010627
PRIORITY APPN. INFO.:			SE 1998-1494	A 19980428
			SE 1998-3954	A 19981118
			WO 1999-SE702	W 19990428

OTHER SOURCE(S): MARPAT 131:317787
 IT 41100-52-1, Memantine hydrochloride
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (NMDA antagonists for treatment of gastrointestinal disorders including irritable bowel syndrome)
 RN 41100-52-1 CAPLUS

L2 ANSWER 24 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
 CN Tricyclo[3.3.1.13.7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 25 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN
 AB The effects of site-specific NMDA receptor antagonists on i.v. cocaine self-administration were examined in rats trained to self-administer cocaine (0.25 mg/infusion) on a fixed ratio (PR) 5 schedule with a 20-s time-out (TO) after each reinforcer. The non-competitive NMDA receptor antagonist dizocilpine (MK-801, (+)-5-methyl-10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5,10-imine hydrogen maleate) (0.05-0.2 mg/kg i.p.) and memantine (1,3-dimethyl-5-amino-adamantane hydrochloride) (2.5-20 mg/kg i.p.), dose-dependently decreased cocaine self-administration, while the competitive NMDA receptor antagonist, CGP 39551 (D(+)-2-amino-4-methyl-5-phosphono-3-pentanoic acid carbonyl ester) (5-15 mg/kg i.p.), and the NMDA/glycine receptor antagonist, L-701,324 (7-[2-(4-hydroxy-3-phenyl)-phenyl]-2(H)quinolone) (1.25-10 mg/kg p.o.), were without effect. Under a progressive ratio (PR) schedule, dizocilpine (0.15 mg/kg i.p.) increased the number of cocaine infusions in a manner similar to increasing the unit dose of cocaine, suggestive of potentiation of cocaine reward. Conversely, memantine (10 mg/kg i.p.) produced rate-decreasing effects on the PR schedule. These results demonstrate that NMDA receptor antagonists acting at different modulatory sites on the NMDA receptor do not share dizocilpine's cocaine reward enhancing effects although they are all known to be effective blockers of NMDA receptor activity.

ACCESSION NUMBER: 1999:546768 CAPLUS

DOCUMENT NUMBER: 131:266935

TITLE: Site-specific NMDA receptor antagonists produce differential effects on cocaine self-administration in rats

AUTHOR(S): Hyttia, Petri; Backstrom, Pia; Liljequist, Sture
 CORPORATE SOURCE: Department of Mental Health and Alcohol Research, National Public Health Institute, Helsinki, FIN-00101, Finland

SOURCE: European Journal of Pharmacology (1999), 378(1), 9-16
 CODEN: EJPHAZ; ISSN: 0014-2999

PUBLISHER: Elsevier Science B.V.

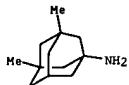
DOCUMENT TYPE: Journal

LANGUAGE: English

IT 41100-52-1
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
 (differential effects of NMDA receptor antagonists on cocaine self-administration in rats)

RN 41100-52-1 CAPLUS

CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS

L2 ANSWER 26 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN
 AB 5-Aminotricyclo[3.3.1.13,7]decanes substituted with either Me or hydrogen in the 1 and/or 3 positions (e.g., 5-aminoadamantane) are prepared in high yield and selectivity by the solvolysis of the corresponding 1,3-substituted 5-(acetamino)adamantanes (e.g., 5-(acetamino)adamantane) with 0.5-1.5 parts alkali (e.g., KOH) in anhydrous MeOH, EtOH, or 2-PrOH for 10-30 h at 110-140°; acid addition salts may be prepared by the reaction of the free amine with (in)organic acids in toluene.

ACCESSION NUMBER: 1999:337632 CAPLUS

DOCUMENT NUMBER: 130:337866

TITLE: Solvolytic process for preparing 1,3-substituted 5-aminotricyclo[3.3.1.13,7]decanes from the corresponding acetamides in the presence of alkali

INVENTOR(S): Kysilka, Vladimir; Bystra, Dagmar; Macoun, Petr; Smekal, Oldrich; Jelinek, Jiri

PATENT ASSIGNEE(S): Lachema A. S., Czech Rep.

SOURCE: Czech Rep., 5 pp.

CODEN: CZXXED

DOCUMENT TYPE: Patent

LANGUAGE: Czech

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CZ 282398	B6	19970716	CZ 1994-863	19940413

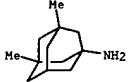
PRIORITY APPN. INFO.: CZ 1994-863

OTHER SOURCE(S): CASREACT 130:337866

IT 41100-52-1P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (solvolytic process for preparing 1,3-substituted 5-aminotricyclo[3.3.1.13,7]decanes from the corresponding acetamides in the presence of alkalis)

RN 41100-52-1 CAPLUS

CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

L2 ANSWER 27 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
 AB The migraine-treating effectiveness of an antimigraine drug is significantly enhanced by administering a selective 5-HT1 agonist together with dextromethorphan or dextrophan.

ACCESSION NUMBER: 1999:231198 CAPLUS

DOCUMENT NUMBER: 130:232532

TITLE: Method for treating migraine using antimigraine drug with 5-HT1 agonist and dextromethorphan or dextrophan

INVENTOR(S): Caruso, Frank S.

PATENT ASSIGNEE(S): Algos Pharmaceutical Corporation, USA

SOURCE: U.S., 6 pp., Cont.-in-part of U.S. Ser. No. 727,923, abandoned.

CODEN: USXOKAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5891885	A	19990406	US 1996-736370	19961024
US 5939425	A	19990817	US 1997-858269	19970519
CA 2267893	AA	19980416	CA 1997-2267893	19971006
WO 9815275	A2	19980416	WO 1997-US17828	19971006
WO 9815275	A3	19980806	WO 1997-US17828	19971006
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
AU 9748061	A1	19980505	AU 1997-48061	19971006
EP 932416	A2	19990804	EP 1997-910772	19971006
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI			
JP 2000050341	T2	20000704	JP 1998-517619	19971006
US 6043244	A	20000328	US 1999-226297	19990107
			US 1996-727923	19961009
PRIORITY APPN. INFO.:			US 1996-736370	A3 19961024
			WO 1997-US17828	W 19971006

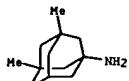
IT 41100-52-1, Menantine hydrochloride

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(antimigraine drug with 5-HT1 agonist and dextromethorphan or dextrophan for migraine treatment)

RN 41100-52-1 CAPLUS

CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)

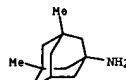


● HCl

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 28 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN
 AB A novel paired transcranial magnetic stimulation (TMS) paradigm with a suprathreshold first and a subthreshold second stimulus was used in healthy volunteers to investigate the acute effects of a single oral dose of various CNS-active drugs on short-interval motor evoked potential (MEP) facilitation. MEPs were recorded from the relaxed abductor digiti muscle. Three peaks of MEP facilitation were consistently observed at interstimulus intervals of 1.1-1.5 ms, 2.3-2.7 ms, and 3.9-4.5 ms. The size of these MEP peaks was transiently suppressed by drugs which enhance gamma-aminobutyric acid (GABA) function in the neocortex (lorazepam, vigabatrin, phenobarbital, ethanol), while the GABA-A receptor agonist baclofen, and -glutamate drugs (gabapentin, memantine), and sodium channel blockers (carbamazepine, lamotrigine), had no effect. The interstimulus intervals effective for the production of the MEP peaks remained unaffected by all drugs. The MEP peaks are thought to be due to a facilitatory interaction of I-(indirect) waves in the motor cortex. Therefore, the present results indicate that the production of I-waves is primarily controlled by GABA related neuronal circuits. The potential relevance of this non-invasive paired TMS protocol for the investigation of I-waves in patients with neurol. disease will be discussed.

ACCESSION NUMBER: 1998:6162/2 CAPLUS
 DOCUMENT NUMBER: 130:423
 TITLE: Pharmacological control of facilitatory I-wave interaction in the human motor cortex. A paired transcranial magnetic stimulation study
 AUTHOR(S): Ziemann, Ulf; Tergau, Frithjof; Wischer, Stephan; Hildebrandt, Jorg; Paulus, Walter
 CORPORATE SOURCE: Department of Clinical Neurophysiology, University of Gottingen, Gottingen, D-37075, Germany
 SOURCE: Electroencephalography and Clinical Neurophysiology (1998), 109(4), 321-330
 CODEN: ECNAEZ; ISSN: 0168-5597
 PUBLISHER: Elsevier Science Ireland Ltd.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 IT 41100-52-1, Memantine hydrochloride
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (pharmacol. control of facilitatory I-wave interaction in the human motor cortex)
 RN 41100-52-1 CAPLUS
 CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)

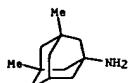


● HCl

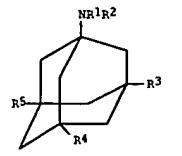
L2 ANSWER 28 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
 REFERENCE COUNT: 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 29 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN
 AB The effects of the GABA receptor antagonists, pentylenetetrazol, bicuculline, and picrotoxin, the glycine antagonist, strychnine, and the NMDA receptor antagonist, memantine, on ethanol-induced behavioral sleep and body temperature were investigated. Pentylenetetrazol, bicuculline, and picrotoxin given prior and following ethanol reduced the behavioral sleep and potentiated the hypothermia caused by ethanol. However, convulsions appeared when bicuculline, but not pentylenetetrazol and picrotoxin, were given following ethanol. After the reversal of unconsciousness in rats without convulsions the animals remained awake throughout the expts. without motor incoordination, hyperexcitability, and sedation, but they were in hypothermia within 12 h. The glycine antagonist, strychnine, given prior or after ethanol had virtually no effect on ethanol-induced behavioral sleep and hypothermia. Ethanol given prior or following strychnine failed to antagonize strychnine-induced convulsions. The NMDA receptor antagonist, memantine, given following ethanol potentiated the behavioral sleep and had virtually no effect on hypothermia induced by ethanol. It is suggested that the ethanol-induced behavioral sleep may be attributed to its ability to enhance the GABAergic mechanisms and to inhibit NMDA-mediated excitatory responses. However, the ethanol-induced hypothermia may be ascribed solely to the facilitation of GABAergic transmission. Further, it is postulated that a bidirectional inhibitory system subserves the regulation of behavioral sleep and convulsions. However, one-way inhibitory system underlies the ethanol-induced hypothermia.

ACCESSION NUMBER: 1997:243380 CAPLUS
 DOCUMENT NUMBER: 126:272263
 TITLE: Opposite effects of GABA and NMDA receptor antagonists on ethanol-induced behavioral sleep in rats
 AUTHOR(S): Belisljin, D. B.; Djokanovid, Nada; Jovanovid-Midic, Danica; Samardzaid, Ranka
 CORPORATE SOURCE: Department of Pharmacology, Medical Faculty, Belgrade, 11000, Yugoslavia
 SOURCE: Alcohol (New York) (1997), 14(2), 167-173
 CODEN: ALCOEX; ISSN: 0741-8329
 PUBLISHER: Elsevier
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 IT 41100-52-1, Memantine hydrochloride
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (effects of GABA and NMDA receptor antagonists on ethanol-induced behavioral sleep and hypothermia in rats)
 RN 41100-52-1 CAPLUS
 CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)



● HCl



AB Adamantane derivs. I (R1, R2 = H, Cl-6 alkyl, or R1NR2 = 5- or 6-membered ring; R3, R4 = H, Cl-6 alkyl, C5-6 cycloalkyl, Ph; R5 = H, Cl-6 alkyl) and their salts are useful for treatment of tinnitus, Meniere's disease, and other inner ear disorders. Thus, patients with cochlear tinnitus were treated with memantine-HCl (10 mg/day by infusion for 5 days, then 20 mg/day by infusion for 5 days, then 20 mg/day orally). Marked improvement was observed in approx 66% of the patients, in some cases the improvement persisted even after discontinuation of treatment.

ACCESSION NUMBER: 1997:148511 CAPLUS
DOCUMENT NUMBER: 1261:166505
TITLE: Adamantane derivatives for treatment of inner ear disorders
INVENTOR(S): Zennner, Hans Peter
PATENT ASSIGNEE(S): Zennner, Hans Peter, Germany
SOURCE: Ger. Offen., 2 pp.
CODEN: GWXEX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

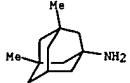
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19528388	A1	19970206	DE 1995-19528388	19950802
CA 2228393	AA	19970213	CA 1996-2228393	19960731
WO 9704762	A1	19970213	WO 1996-EP3360	19960731
	W:	AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LX, LR, LS, LT, LU, LV, MD, MG, MX, HN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, RW: KE, LS, MW, SD, SZ, UG, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG		
AU 9667882	A1	19970226	AU 1996-67882	19960731
AU 719018	B2	20000504		
EP 759295	A1	19970226	EP 1996-112325	19960731
EP 759295	B1	19980304		
	R:	AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE		
AT 163545	E	19980315	AT 1996-112325	19960731
EP 834310	A1	19980408	EP 1997-122113	19960731

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI
ES 2116801 T3 19980716 ES 1996-112325 19960731
CN 1194581 A 19980930 CN 1996-196650 19960731
BR 9609950 A 19990629 BR 1996-9950 19960731
JP 2000515486 T2 20001121 JP 1997-507250 19960731
JP 3560039 B2 20040922
IL 123142 A1 20011031 IL 1996-123142 19960731
US 6066652 A 20000523 US 1998-11085 19980612
PRIORITY APPLN. INFO.: DE 1995-19528388 A 19950802
EP 1996-112325 A3 19960731
WO 1996-EP3360 W 19960731

OTHER SOURCE(S): MARPAT 126:166505

IT 41100-52-1, Memantine hydrochloride
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adamanthane derivs. for treatment of inner ear disorders)

RN 41100-52-1 CAPLUS
CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

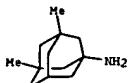
AB N-terminal Fmoc-protected peptide combinations that form gels in water and diverse organic solvents. These types of peptides form gels in aqueous solns. and are biol. compatible and may be useful for drug delivery, antigen delivery and may be useful as food additives to retard spoilage and act as fillers. A gel containing 10 mg/mL Fmoc-Leu-Asp was prepared and 5-methyl-1-adamanthamine-3-carboxylic acid (I) was incorporated into the buffered saline was injected into rabbits, without adjuvant, antibodies were raised against this drug to produce antisera with titers as high or higher than those of animals immunized with I-bovine serum albumin conjugates in equal vols. of complete Freund's adjuvant.

ACCESSION NUMBER: 1995:863630 CAPLUS
DOCUMENT NUMBER: 123:266122
TITLE: Gel-forming polypeptide derivatives for drug delivery
INVENTOR(S): Vegers, Roland; Janney, Paul A.
PATENT ASSIGNEE(S): Brigham and Women's Hospital, USA
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9521622	A1	19950817	WO 1995-US1890	19950209
	W:	AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LX, LR, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US		
	RW:	KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG		
AU 9519195	A1	19950829	AU 1995-19195	19950209
JP 10511340	T2	19981104	JP 1995-521421	19950209
US 5955434	A	19990921	US 1996-693215	19960809
PRIORITY APPLN. INFO.:			LV 1970-700000	A 19940209
			LV 1994-940007	A 19940209
			WO 1995-US1890	W 19950209

OTHER SOURCE(S): MARPAT 123:266122
IT 41100-52-1
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gel-forming polypeptide derivs. for drug delivery)

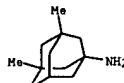
RN 41100-52-1 CAPLUS
CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

L2 ANSWER 32 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN
 AB The activation of glutamate receptors by endogenous glutamate has been implicated in the processes that underlie cell loss associated with ischemia and trauma and in the development of some neurodegenerative diseases. The antagonism of NMDA-sensitive glutamate receptors may therefore have therapeutic applications. The present study compared the side effects and neuroprotective potency of 1-aminoadamantane hydrochloride (amantadine), 1-amino-3,5-dimethyladamantane hydrochloride (memantine), and (+)-5-methyl-10,11-dihydro-5H-dibenzo[b,e]cyclohepten-5,10-imine maleate ((+)-MK-801) against NMDA injected directly into the nucleus basalis magnocellularis of rats. Each drug significantly attenuated the loss of nucleus basalis magnocellularis cholinergic cells. The ED50s were resp. 0.077, 2.81 and 43.5 μ g/kg for (+)-MK-801, memantine and amantadine, giving a relative potency ratio of 1:36:565. The ratio of the ED50 for the side effects observed, including ataxia, hyporeflexia and stereotypy, and the ED50 for neuroprotective ability, was highest for memantine and the lowest for (+)-MK-801. The results suggest that a potential neuroprotective action of NMDA receptor antagonists, memantine and amantadine in particular, can be seen at low doses lacking side effects.

ACCESSION NUMBER: 1995:847129 CAPLUS
 DOCUMENT NUMBER: 123:275847
 TITLE: MK-801, memantine and amantadine show neuroprotective activity in the nucleus basalis magnocellularis
 AUTHOR(S): Wink, Gary L.; Danyz, Wojciech; Mobley, Sherri L.
 CORPORATE SOURCE: Arizona Research Laboratories Division of Neural Systems, Memory and Aging, 384 Life Sciences North, University of Arizona, Tucson, AZ, USA
 SOURCE: European Journal of Pharmacology, Environmental Toxicology and Pharmacology Section (1995), 293(3), 267-70
 CODEN: EPEPEG; ISSN: 0926-6917
 PUBLISHER: Elsevier
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 IT 41100-52-1, Memantine hydrochloride
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (NMDA receptor antagonists MK-801 and memantine and amantadine show neuroprotective activity in nucleus basalis magnocellularis injury induced by NMDA)
 RN 41100-52-1 CAPLUS
 CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)

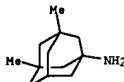


● HCl

L2 ANSWER 33 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN
 AB CA1 pyramidal cell response (population spike) in the hippocampal slice preparation was monitored after elec. stimulation of the Schaffer collaterals

at CA2 in the presence of different concns. of memantine (1-amino-3,5-dimethyladamantane, Akatinol Memantine, CAS 41100-52-1) currently being prescribed for the treatment of e.g. dementia. Memantine increased the amplitude of the population spike by 100% compared to the predrug level with an EC50 of approx. 8 μ mol/l. Long-term potentiation induced by a brief theta stimulus was likewise increased by a factor of 2. The concentration dependent action of D-serine, an agonist acting at the strychnine insensitive glycine-site of the NMDA (N-methyl-D-aspartic acid) receptor was enhanced in the presence of 1 μ mol/l of memantine. These effects of memantine were antagonized completely by very low concns. of the selective non-NMDA receptor antagonist NBQX (2,3-dihydroxy-6-nitro-7-sulfamoyl-benzof (F) quinoxaline) as well as by less selective antagonist such as DNX (6,7-dinitroquinoxaline-2,3-dione) and CNQX (6-cyano-7-nitroquinoxaline-2,3-dione). In contrast, dizocilpine tested under identical conditions and in concordance with the literature decreased long-term potentiation. Thus, memantine clearly has different effects on glutamatergic synaptic transmission compared to dizocilpine. The ability of memantine to enhance synaptic transmission in the hippocampus is in concordance with the reported pos. influence on cognition deficits in humans.

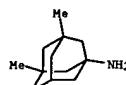
ACCESSION NUMBER: 1995:411501 CAPLUS
 DOCUMENT NUMBER: 122:178277
 TITLE: Effects of memantine on synaptic transmission in the hippocampus in vitro
 AUTHOR(S): Dimpfel, W.
 CORPORATE SOURCE: Pro Sci. Private Res. Inst. GmbH, Linden, Germany
 SOURCE: Arzneimittel-Forschung (1995), 45(1), 1-5
 CODEN: ARZNAD; ISSN: 0004-4172
 PUBLISHER: Cantor
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 IT 41100-52-1, Memantine hydrochloride
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (memantine effect on synaptic transmission in the hippocampus)
 RN 41100-52-1 CAPLUS
 CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

L2 ANSWER 34 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN
 AB The competitive N-methyl-D-aspartate (NMDA) receptor antagonists, DL-(E)-2-amino-4-methyl-5-phosphonovaleric acid (CGP 37849) and DL(-)-2-amino-5-phosphonovaleric acid (APV), and the non-competitive NMDA antagonists, memantine and amantadine, which are used in the treatment of Parkinson's disease, were tested for their effects on intrastriatally evoked excitatory postsynaptic potentials (EPSPs) in rat neostriatal slices. Fast, non-NMDA receptor mediated synaptic excitation was not affected by any of the NMDA receptor antagonists. The NMDA component of the EPSPs was more prominent following reduction of the non-NMDA component of the EPSP by the non-NMDA receptor antagonist 6-cyano-7-nitroquinoxaline-2,3-dione (CNQX, 5-10 μ M). Memantine (30 μ M) and amantadine (100 μ M) had similar effects in reducing the NMDA component, but were not as effective as CGP 37849 (1-5 μ M) or APV (10 μ M). The data are compatible with a possible locus of action of memantine and amantadine in the neostriatum.

ACCESSION NUMBER: 1995:276696 CAPLUS
 DOCUMENT NUMBER: 122:46388
 TITLE: Suppression by memantine and amantadine of synaptic excitation intrastriatally evoked in rat neostriatal slices
 AUTHOR(S): Rohrbacher, Jutta; Bijak, Maria; Misgeld, Ulrich
 CORPORATE SOURCE: I. Physiologisches Inst., Universitaet Heidelberg, Heidelberg, D-69120, Germany
 SOURCE: Neuroscience Letters (1994), 182(1), 95-8
 PUBLISHER: Elsevier
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 IT 41100-52-1, Memantine, hydrochloride
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (suppression by NMDA receptor antagonists memantine and amantadine of synaptic excitation intrastriatally evoked in rat neostriatal slices in relation to Parkinson's disease treatment)
 RN 41100-52-1 CAPLUS
 CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)



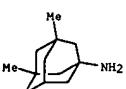
● HCl1

L2 ANSWER 35 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN
 AB Nonischemic NMDA receptor-mediated neuronal damage in a mammal is reduced by administering amantadine and related compds. to the mammal. Also disclosed is a screen for antagonists of NMDA receptor-mediated neurotoxicity which have an enhanced prospect for being clin. tolerated and selective against such neurotoxicity. The amantadine derivative, memantine, prevented retinal ganglion cell death from the endogenous glutamate-related toxin in a dose-dependent manner.

ACCESSION NUMBER: 1994:261373 CAPLUS
 DOCUMENT NUMBER: 120:261373
 TITLE: Method of preventing NMDA receptor-mediated neuronal damage using amantadine and related compounds
 INVENTOR(S): Lipton, Stuart A.
 PATENT ASSIGNEE(S): The Children's Medical Center Corp., USA
 SOURCE: PCT Int. Appl., 28 pp.
 CODEN: PIKXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 10
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9405275	A1	19940317	WO 1993-US8344	19930903
W: AU, CA, JP RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5334618	A	19940802	US 1992-939824	19920903
AU 9348476	A1	19940329	AU 1993-48476	19930903
EP 660707	A1	19950705	EP 1993-921355	19930903
EP 660707	B1	20010627		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 08501297	T2	19960213	JP 1993-507482	19930903
AT 202474	E	20010715	AT 1993-921355	19930903
GR 3036657	T3	20011231	GR 2001-401515	20010918
PRIORITY APPLN. INFO.:			US 1992-939824	A 19920903
			US 1991-680201	B2 19910404
			WO 1993-US8344	W 19930903

IT 41100-52-1, Memantine hydrochloride
 RL: BIOL (Biological study)
 (retinal ganglion cell death from glutamate-related toxin prevention by)
 RN 41100-52-1 CAPLUS
 CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)



● HCl1

L2 ANSWER 36 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN
 AB A dosage form with matrix-controlled 2-stage release of the active ingredient has a matrix comprising a mixture of water-soluble and water-insol.

casein salts. The matrix is produced by mixing the water-soluble and water-insol. casein salts or by adding salts of di- or multivalent cations to water-soluble casein. Thus, tablets were prepared containing memantine-HCl 20.0, Na caseinate 46.8, Ca caseinate 31.2, Aerosil 200 1.0, and Mg stearate 1.0 weight%.

ACCESSION NUMBER: 1994:144211 CAPLUS
 DOCUMENT NUMBER: 120:144211
 TITLE: Process for producing solid pharmaceutical dosage forms with an extended two-stage release
 INVENTOR(S): Huenberg, Eberhard; Seiller, Erhard; Ritsert, Stefan
 PATENT ASSIGNEE(S): Herz & Co. G.m.b.H. und Co., Germany
 SOURCE: Eur. Pat. Appl., 11 pp.
 CODEN: EPXXDW

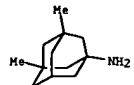
DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 592186	A1	19940209	EP 1993-112018	19930728
EP 592186	B1	19990224		
RU, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE	A1	19940210	DE 1992-4225730	19920804
DE 4225730	C2	20030430		
DE 4225730	A	19950117	US 1993-96952	19930723
AT 17666	E	19990315	AT 1993-112018	19930728
ES 2128369	T3	19990516	ES 1993-112018	19930728
ZA 9305614	A	19950203	ZA 1993-5614	19930803
IN 176667	A	19960817	IN 1993-HA538	19930803
IL 106580	A1	19980208	IL 1993-106580	19930803
WO 9403158	A1	19940217	WO 1993-EP2074	19930804
AU, BR, CA, CZ, FI, HU, JP, KR, NO, PL, RU, SK, UA	A	19940518	CN 1993-116211	19930804
CN 1086708	A	19950327	LT 1993-833	19930804
LT 320	B	19950420	LV 1993-1013	19930804
LV 10182	B	19951019	JP 1994-505015	19930804
JP 07509479	T2	19951019		
JP 3560244	B2	20040902		
AU 665131	B2	19960620	AU 1993-47069	19930804
AU 9347069	A1	19940303	DE 1992-4225730	A 19920804
PRIORITY APPLN. INFO.:			WO 1993-EP2074	W 19930804

IT 41100-52-1, Memantine hydrochloride
 RL: BIOL (Biological study)
 (controlled-release pharmaceuticals containing, casein water-insol. and water-soluble salts in)
 RN 41100-52-1 CAPLUS
 CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)

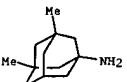
L2 ANSWER 36 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



● HCl

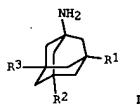
L2 ANSWER 37 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN
 AB A recently developed solid-phase binding assay was used to investigate the specificity of ligand binding to a mouse monoclonal anti-dinitrophenol IgE (I). All DNP-amino acids, that were tested inhibited the binding of the radio-labeled I to DNP covalently attached to polystyrene microplates; however, the concentration for 50% inhibition varied within four orders of magnitude, DNP-L-serine being the most and DNP-L-proline the least potent inhibitor. In addition to DNP analogs, a large number of drugs and other compds. were tested for their ability to compete with DNP for the binding site of I. At the concentration used for screening, 59% of compds. had no significant inhibition; 19% inhibited the binding of I more than 50%. Several families of compds. (tetracyclines, polymyxins, phenothiazines, salicylates, and quinones) that were effective competitors were found. Within these families, changes in the functional groups attached to the family stem had major effects on the affinity of ligand binding. The occurrence frequencies of interactions of ligands with I is in good agreement with the semi-empirical model for multispecific antibody-ligand interactions.

ACCESSION NUMBER: 1992:00277 CAPLUS
 DOCUMENT NUMBER: 117:277
 TITLE: Mechanism of allergic cross-reactions. I. Multispecific binding of ligands to a mouse monoclonal anti-DNP IgE antibody
 AUTHOR(S): Varga, Janos M.; Kalchschmid, Gertrud; Klein, Georg F.; Fritsch, Peter
 CORPORATE SOURCE: Dep. Dermatol., Univ. Innsbruck, Innsbruck, 6020, Austria
 SOURCE: Molecular Immunology (1991), 28(6), 641-54
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 IT 41100-52-1, Memantine hydrochloride
 RL: BIOL (Biological study)
 (binding of, to anti-dinitrophenol monoclonal antibody, allergic cross-reaction mechanism in relation to)
 RN 41100-52-1 CAPLUS
 CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)



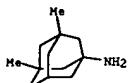
● HCl

L2 ANSWER 38 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN



AB A series of bridgehead substituted amantadines I (R1-3 = H, Me; R1-2 = Me, Et, R3 = H; R1 = Me, Et, Pr, R2-3 = H) were prepared and tested for potential antiparkinson activity as dopamine agonists (DA). E.g., 1,3-adamantanedicarboxylic acid was converted to its di-Me ester, which was reduced with LiAlH4 to give 83.5% 1,3-adamantanediethanol, which was successively tosylated and reduced to give 1,3-diethyladamantane (II). Bromination of II gave 83.8% 3,5-diethyl-1-bromoadamantane, which was successively treated with AcNH2 and KOH to give I (R1-2 = Et, R3 = H). The compds. were evaluated (DA) using a battery of three murine bioassays, including stimulation of locomotor activity, induction of circling in animals with unilateral striatal lesions, and reversal of reserpine α -methyltyrosine induced akinesia. Apparent mechanistic differences were seen between the Me-substituted series and the Et-substituted series. While activities in both series increase with increasing lipophilicity, the Me series as well as amantadine itself, exhibits only indirect DA agonist activity, as evidenced by ipsilateral rotation in the circling model and no significant difference from control in reversal of akinesia. The Et series exhibits weak but reproducible direct DA agonist activity, as shown by contralateral rotation in the circling assay for I (R1 = Et, R2-3 = H) and reversal of akinesia by I (R1 = Et; R2-3 = H; R1-2 = Et, R3 = H). I (R1 = Pr, R2-3 = H) was devoid of any DA agonist activity.

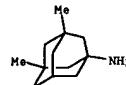
ACCESSION NUMBER: 1982:19721 CAPLUS
 DOCUMENT NUMBER: 96:19721
 TITLE: Structure-anti-Parkinson activity relationships in the aminoadamantanes. Influence of bridgehead substitution
 AUTHOR(S): Henkel, James G.; Hane, Jeffrey T.; Gianutsos, Gerald Sch. Pharm., Univ. Connecticut, Storrs, CT, 06268, USA
 CORPORATE SOURCE: Journal of Medicinal Chemistry (1982), 25(1), 51-6
 SOURCE: CODEN: JMCMAR; ISSN: 0022-2623
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 96:19721
 IT 41100-52-1P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)
 RN 41100-52-1 CAPLUS
 CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)



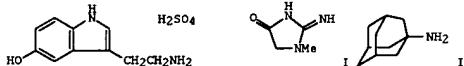
● HCl

L2 ANSWER 39 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN
 AB Human blood platelets were incubated with drugs which either liberated only 5-HT [50-67-9] (incomplete release reaction) or 5-HT as well as ATP [156-65-5]/ADP [58-64-0] (complete release reaction) from subcellular storage organelles. The incomplete release reaction induced by tyramine [51-67-2], tryptamine [61-54-1], and 1-aminoadamantane-HCl [665-66-7] was followed by an increased 5-HT uptake which was enhanced up to 350% as compared with the untreated platelets. After treatment with drugs like 1-amino-3,5-dimethyladamantane-HCl [41100-52-1], imipramine [50-49-7], and reserpine [50-55-5], which induced the complete release reaction, platelets took up significantly less 5-HT as compared with the controls. Apparently, the metabolically inert ATP within the storage organelles is necessary for 5-HT uptake and storage. The uptake of radioactively labeled adenine [73-24-5] and the synthesis of metabolically active adenine nucleotides were increased after preincubation with both types of release-inducing substances. The newly synthesized ATP may serve to restore the metabolically active, cytoplasmic ATP which is consumed either for the extrusion process during the complete release reaction or for the energy-requiring 5-HT reuptake observed after treatment with 5-HT displacing agents.

ACCESSION NUMBER: 1981:417954 CAPLUS
 DOCUMENT NUMBER: 95:17964
 TITLE: 5-Hydroxytryptamine and adenine uptake by human blood platelets following the release reaction
 AUTHOR(S): Wesemann, W.; Von Pusch, I.
 CORPORATE SOURCE: Inst. Physiol. Chem., Philipps-Univ. Marburg, Marburg, Fed. Rep. Ger.
 SOURCE: Thrombosis Research (1981), 21(4-5), 367-74
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 IT 41100-52-1
 RL: BIOL (Biological study)
 (blood platelet uptake of adenine and hydroxytryptamine response to)
 RN 41100-52-1 CAPLUS
 CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)

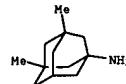


● HCl

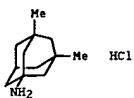


AB Rat brain synaptosomes incorporated serotonin creatinine sulfate (I) [971-74-4] with 2 different uptake mechanisms, high affinity: $K_1 = 47 \text{ nM}$ and low affinity: $K_2 = 660 \text{ nM}$. Both uptake mechanisms were noncompetitively inhibited by the potential antiparkinson drugs 1-aminoadamantane-HCl (II-HCl) [665-66-7] ($K_1 = 57 \mu\text{M}$, $K_2 = 96 \mu\text{M}$) and 1-amino-3,5-dimethyladamantane-HCl (III) [41100-52-1] ($K_1 = 97 \mu\text{M}$, $K_2 = 150 \mu\text{M}$). The incorporated I was released from synaptosomes on incubation with high concns. (0.5-5 mM) of the drugs or on elec. stimulation with rectangular pulse of alternating polarity. Subthreshold concns. of these drugs (5-50 μM) which are too low to liberate I increased the elec. stimulated release of I. The effect of II, III, and elec. stimulation on dopamine [51-61-6] release paralleled the results observed with I. The uptake of I into isolated synaptic vesicles and the binding to isolated nerve ending membranes was noncompetitively inhibited by 1-aminoadamantanes. III inhibited the binding of I to membranes more effectively ($K_i = 0.95 \text{ mM}$) than its uptake into vesicles ($K_i = 1.2 \text{ mM}$) contrasting with II which was a weaker inhibitor affecting vesicular uptake ($K_i = 2.5 \text{ mM}$) slightly more than membrane binding ($K_i = 3.1 \text{ mM}$). In addition to other mechanisms like receptor stimulation, 1-aminoadamantanes may act in parkinsonian patients by enriching the transmitter content in the synaptic cleft.

ACCESSION NUMBER: 1979:432708 CAPLUS
 DOCUMENT NUMBER: 91:32708
 TITLE: In vitro studies on the possible effects of 1-aminoadamantanes on the serotonergic system in parkinsonism
 AUTHOR(S): Wesemann, W.; Dette-Wildenhehn, G.; Fellehner, H.
 CORPORATE SOURCE: Physiol.-Chem. Inst. II, Philipps-Univ., Marburg/Lahn, Fed. Rep. Ger.
 SOURCE: Journal of Neural Transmission (1972-1989) (1979), 44(4), 263-85
 CODEN: JNTMAH; ISSN: 0300-9564
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 IT 41100-52-1
 RL: BIOL (Biological study)
 (serotonin metabolism by brain synaptosomes response to)
 RN 41100-52-1 CAPLUS
 CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)



● HCl



I

AB The effects of memantine (1,3-dimethyl-5-aminoadamantane hydrochloride) (I) [41100-52-1] (10 mg/kg, i.v.) on the stretch-induced reflex tension of flexor muscles extensor digitorum longus and tibialis anterior (EDL/TA) and on the excitability of the neurons relaying transmission in the γ -loop were investigated in decerebrate and spinal cats. I essentially reduced the reflex excitability of flexors EDL/TA induced by fusimotor activity in the decerebrate preparation. The drug did not stimulate the reflex activity in acute spinal cats. I suppressed largely the transmission of the fusimotor reflex in the decerebrate as well as in the spinal preparation, although in spinal cats I increased the average firing rate of muscle spindle primaries originating from EDL/TA muscles. The possible mechanism of action of the compound on dopaminergic and serotonergic systems as well as its basic effects on neuronal membranes is discussed.

ACCESSION NUMBER: 1977:545745 CAPLUS

DOCUMENT NUMBER: 87:145745

TITLE: Effects of 1,3-dimethyl-5-aminoadamantane hydrochloride (DMAA) on the stretch-induced reflex tension of flexor muscles and the excitability of the γ -loop in decerebrate and spinal cats

AUTHOR(S): Wand, P.; Sontag, K. H.; Cremer, H.

CORPORATE SOURCE: Dep. Biochem. Pharmacol., Max-Planck-Inst. Exp. Med., Goettingen, Fed. Rep. Ger.

SOURCE: Arzneimittel-Forschung (1977), 27(7), 1477-81

CODEN: ARZNAD; ISSN: 0004-4172

DOCUMENT TYPE: Journal

LANGUAGE: English

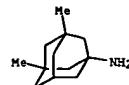
IT 41100-52-1

RL: BIOL (Biological study)
(muscle stretch reflex response to, in decerebrate and spinal animals,
 γ -motor neurons in relation to)

RN 41100-52-1 CAPLUS

CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA

INDEX NAME)



● HCl

AB The effects of memantine (1,3-dimethyl-5-aminoadamantane hydrochloride) (I) [41100-52-1] (10 mg/kg, i.v.) on the stretch-induced reflex tension of flexor muscles extensor digitorum longus and tibialis anterior (EDL/TA) and on the excitability of the neurons relaying transmission in the γ -loop were investigated in decerebrate and spinal cats. I essentially reduced the reflex excitability of flexors EDL/TA induced by fusimotor activity in the decerebrate preparation. The drug did not stimulate the reflex activity in acute spinal cats. I suppressed largely the transmission of the fusimotor reflex in the decerebrate as well as in the spinal preparation, although in spinal cats I increased the average firing rate of muscle spindle primaries originating from EDL/TA muscles. The possible mechanism of action of the compound on dopaminergic and serotonergic systems as well as its basic effects on neuronal membranes is discussed.

ACCESSION NUMBER: 1977:545745 CAPLUS

DOCUMENT NUMBER: 87:145745

TITLE: Effects of 1,3-dimethyl-5-aminoadamantane hydrochloride (DMAA) on the stretch-induced reflex tension of flexor muscles and the excitability of the γ -loop in decerebrate and spinal cats

AUTHOR(S): Wand, P.; Sontag, K. H.; Cremer, H.

CORPORATE SOURCE: Dep. Biochem. Pharmacol., Max-Planck-Inst. Exp. Med., Goettingen, Fed. Rep. Ger.

SOURCE: Arzneimittel-Forschung (1977), 27(7), 1477-81

CODEN: ARZNAD; ISSN: 0004-4172

DOCUMENT TYPE: Journal

LANGUAGE: English

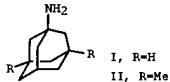
IT 41100-52-1

RL: BIOL (Biological study)
(muscle stretch reflex response to, in decerebrate and spinal animals,
 γ -motor neurons in relation to)

RN 41100-52-1 CAPLUS

CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA

INDEX NAME)



I, R=H

II, R=Me

AB Amantadine-HCl (I-HCl) [665-66-7] and D-145-HCl (II-HCl) [41100-52-1] administered either i.p. or orally to rats at 50-100 mg/kg were rapidly absorbed. Between 20 and 25% I and 6-11% II were excreted unchanged in the urine, this excretion being maximum 2 h after administration. 1-Amino-3-hydroxyadamantane [702-82-9] was the only I metabolite detected, whereas 1-hydroxy-3,5-dimethyladamantane [707-37-9], 1-amino-3-hydroxymethyl-5-methyladamantane [58850-55-8], 1-amino-4-hydroxy-3,5-dimethyladamantane [58850-54-7], and 1-amino-7-hydroxy-3,5-dimethyladamantane [63971-25-5] were II metabolites. Following oral administration of 10 mg II to a human volunteer, I and 1-amino-3-hydroxymethyl-5-methyladamantane were excreted in the urine.

ACCESSION NUMBER: 1977:526940 CAPLUS

DOCUMENT NUMBER: 87:126940

TITLE: Gas chromatographic and mass spectrometric studies on metabolites of amino adamantanone excreted in urine

AUTHOR(S): Wesemann, W.; Schollmeyer, J. D.; Sturm, G.
Inst. Physiol. Chem. II, Philipps-Univ., Marburg, Fed. Rep. Ger.CORPORATE SOURCE: Arzneimittel-Forschung (1977), 27(7), 1471-7
CODEN: ARZNAD; ISSN: 0004-4172

DOCUMENT TYPE: Journal

LANGUAGE: German

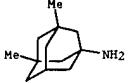
IT 41100-52-1

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(metabolism of)

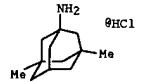
RN 41100-52-1 CAPLUS

CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA

INDEX NAME)



● HCl



I

AB Nerve endings isolated from rat brain accumulated exogenous serotonin [50-67-9] and dopamine [51-61-6]. Both biogenic amines were released by elec. stimulation and by incubation with $5 \times 10^{-5} - 5 \times 10^{-4}$ M 1-aminoadamantane-HCl [665-66-7] and 1-amino-3,5-dimethyladamantane-HCl (I) [41100-52-1]; the elec.-stimulated release was small and could be significantly increased after simultaneous incubation of nerve endings with subthreshold concns. ($5 \times 10^{-6} - 5 \times 10^{-5}$ M) of the adamantane derivs. The reuptake of released serotonin was noncompetitively inhibited by the adamantanes. Serotonin uptake by blood platelets was also inhibited by small concns. of I ($10^{-5} - 2 \times 10^{-4}$ M). High I concns. ($> 2 \times 10^{-3}$ M) induced simultaneous release of serotonin, ATP [56-65-5], and ADP [59-64-0]. At $2 \times 10^{-4} - 2 \times 10^{-3}$ M I, only serotonin was released.

ACCESSION NUMBER: 1977:511437 CAPLUS

DOCUMENT NUMBER: 87:111437

TITLE: Effect of 1-aminoadamantanes. Comparative investigations with isolated nerve endings and blood

AUTHOR(S): Haacke, U.; Sturm, G.; Suauer, V.; Wesemann, W.; Wildenbahn, G.

CORPORATE SOURCE: Physiol.-Chem. Inst. II, Philipps-Univ., Marburg, Fed. Rep. Ger.

SOURCE: Arzneimittel-Forschung (1977), 27(7), 1481-7
CODEN: ARZNAD; ISSN: 0004-4172

DOCUMENT TYPE: Journal

LANGUAGE: German

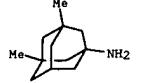
IT 41100-52-1

RL: BIOL (Biological study)
(dopamine and serotonin release by blood platelet and brain nerve endings response to)

RN 41100-52-1 CAPLUS

CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA

INDEX NAME)



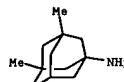
● HCl

L2 ANSWER 44 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN
 GI For diagram(s), see printed CA Issue.
 AB Eight adamantananes (I, R = NH₂, NHMe, NMe₂, NMeCHMe₂, or cyclohexylamino; R₁, R₂ = Cl-4-alkyl) and their salts, used in the treatment of parkinsonism, were prepared from I (R = Cl or Br) and urea and derivs. The activity of I, HCl (R = NMe₂, R₁ = R₂ = Me) (II, HCl) in the central nervous system was tested i.p. in the mouse and rat. Thus, I (R = Cl, R₁ = R₂ = Me) and urea were heated at 220° to give, after treatment with HCl, 78% II, HCl. Methylation of II with HCHO and HCO₂H gave, after HCl-treatment, 77% I (R = NMe₂, R₁ = R₂ = Me).

ACCESSION NUMBER: 1975-86248 CAPLUS
 DOCUMENT NUMBER: 82:86248
 TITLE: 3,5-Dialkyl-1-aminoadamantanes for the treatment of parkinsonism
 INVENTOR(S): Schern, Arthur; Peteri, Dezsö
 PATENT/ASSIGNEE(S): Herz und Co.
 SOURCE: Ger. Offen., 20 pp.
 CODEN: GWXXBX
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2318461	A1	19741031	DE 1973-2318461	19730412
BE 798450	A1	19730816	BE 1973-130199	19730419
NL 7305644	A	19731023	NL 1973-5644	19730419
AT 7303530	A	19750815	AT 1973-3530	19730419
AT 329532	B	19760510		
CA 974518	A1	19750916	CA 1973-169484	19730419
ES 413944	A1	19760601	ES 1973-413944	19730419
PL 89158	P	19761030	PL 1973-162028	19730419
CH 603545	A	19780831	CH 1973-5686	19730419
FR 2182998	A1	19731214	FR 1973-14690	19730420
JP 49018860	A2	19740219	JP 1973-44965	19730420
US 4122193	A	19781024	US 1973-352893	19730420
GB 1393503	A	19750507	GB 1973-19436	19730424
PRIORITY APPLN. INFO.:			DE 1972-2219256	19720420
			DE 1973-2318461	A 19730412

IT 41100-52-1P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation and use in the treatment of parkinsonism)
 RN 41100-52-1 CAPLUS
 CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)

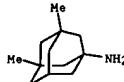


● HCl

L2 ANSWER 45 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN
 GI For diagram(s), see printed CA Issue.
 AB Aminoadamantanes (I, R = Me, Et; R₁, R₂, R₃ = H, Me) were prepared by treating halo adamantananes (II) with R₃NHCONHR₃ at 165-85°.

ACCESSION NUMBER: 1973:124152 CAPLUS
 DOCUMENT NUMBER: 78:124152
 TITLE: Aminoadamantanes and their salts
 INVENTOR(S): Burkhardt, Jiri; Landa, Stanislav
 SOURCE: Czech., 3 pp.
 CODEN: CZXXA9
 DOCUMENT TYPE: Patent
 LANGUAGE: Czech
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CS 146405		19721215	CS 1970-5509	19700806
IT 41100-52-1P				
RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of)				
RN 41100-52-1 CAPLUS				
CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)				



● HCl

AB To assess the possible pharmacodynamic effects of the sym. lipophilic adamanyl group, a number of N-arylsulfonyl-N'-adamantylureas, $\text{ArSO}_2\text{NHCONHR}$ (I), were prepared for evaluation as hypoglycemic agents. (All s.p.s. were taken in sealed, submerged capillary tubes.) Adamantane-1-carboxamide (9 g.) in 200 ml. dry Et₂O added to 10 g. LiAlH₄ suspended in 500 ml. dry Et₂O with stirring, the mixture refluxed 4 hrs., cooled to -5° with stirring, treated dropwise by 10 ml. H₂O, followed by 30 ml. 10% aqueous NaOH

and 10 ml. H₂O, the solids filtered off and washed with 500 ml. Et₂O, the combined Et₂O solns. dried and evaporated in vacuo, the residue dissolved in 50 ml. Et₂O, and the solution filtered and treated with dry HCl gave 7 g. 1-amino-3-methyladamantane-HCl, m. 320° (EtOH). 1-Methyladamantane brominated by the procedure reported for 1-bromoadamantane (Stetter, et al., CA 53, 21709f; 54, 1356a) gave 93% 3-methyl-1-bromoadamantane (II), b.p. 65-7°, whose structure was supported by its nuclear magnetic resonance (n.m.r.) spectrum. From II was prepared by the $\text{HgCl}_2\text{HgSO}_4$ method (5., et al., CA 54, 9950d) 1-acetamido-3-methyladamantane (III), m. 108-9° (sublimation at 90-100°/0.05 mm.). Deacetylation of III by KOH in $\text{O}(\text{CH}_2\text{CH}_2\text{OH})_2$, followed by Et₂O extraction gave an Et₂O solution containing product and approx. 5% unchanged III, which was treated with dry HCl

to give 87% 1-amino-3-methyladamantane-HCl, m. 295-300°. 1,3-Dimethyladamantane brominated as above gave 77.5 g. 1-bromo-3,5-dimethyladamantane (IV), b.p. 60-67°, n_D²⁵ 1.5178 (structure supported by n.m.r. spectrum), which was converted into 96% 1-acetamido analog of IV, m. 80-2° (sublimation), and the latter into 87% 1-amino analog of IV, HCl salt, m. 290-5°. Adamantane (V) (100 g.) and 85 g. *tert*-BuCl in 400 ml. anhydrous cyclohexane treated portionwise during 8 hrs. with 4.6 g. (total) AlCl₃ (in 0.5 g. batches AlCl₃), when the reaction was complete (as judged from escaping isobutane gas), 100 ml. N HCl added with stirring, followed by 500 ml. Et₂O, and the organic layer separated, washed with 50 ml. cold H₂O and 50 ml. 5% aqueous NaHCO₃, dried, and evaporated in vacuo gave 115 g. crude 1-chloroadamantane (VI), m. 152-6°, containing (gas chromatography) 90-5% VI and 5-10% VI recryst. of a sample from EtOH at -50° gave pure VI, as determined by mixed m.p. with authentic VI and by x-ray diffraction patterns. Crude VI was converted by the MeCN-HgSO_4 method into 83% crude 1-acetamidoadamantane (VII), m. 144-6°; pure VII m. 147-9° (EtOH). Crude VII (108 g.) saponified gave 51 g. pure 1-aminoadamantane (VIII), m. 160-200°. VIII (302.5 g.) and 535 g. 4-MeC₆H₄SO₂NHCO₂Et in 6 l. dry PhMe refluxed 5 hrs., cooled to room temperature, the crystalline solid filtered off and dissolved

(without application of heat) in approx. 2 l. CHCl₃ which had previously been shaken with 50 g. Al₂O₃ to remove traces EtOH, the solution washed with cold 5% HCl and H₂O until neutral, dried (MgSO₄), concentrated in vacuo to 1/2

its volume, warmed to 50°, diluted with hot petr. ether (b.p. 60-71°) to start crystallization, and chilled overnight gave 400 g. I (Ar = 4-MeC₆H₄, R = 1-adamantyl) (IX), m. 178-9° (CHCl₃-petr. ether). The following I were prepared (Ar, R, m.p., relative potency with respect to hypoglycemic activity given): 4-MeC₆H₄, Bu (Tolbutamide), -, 1; 4-MeC₆H₄, 1-adamantyl, 178-9°, 15.5; 4-MeC₆H₄, cyclohexyl (Tolcyclamide), -, 12.8; 4-EtC₆H₄, 1-adamantyl, 153-5°, 14.8; 4-EtC₆H₄, cyclohexyl, -, 9.3; 4-MeSC₆H₄, 1-adamantyl, 155-8°, 8.7; 4-MeSC₆H₄, cyclohexyl (Thiohexamide), -, 4.1; 4-ClC₆H₄, 1-adamantyl, 150-1°, 5.1; 4-ClC₆H₄, cyclohexyl, -, 5.6; 4-ClC₆H₄, Pr, -, 2.1; 4-iso-PrC₆H₄, 1-adamantyl, 190-2°, 2.9; 4-AcC₆H₄, 1-adamantyl, 163-5°,

1,6; 4-AcC₆H₄, cyclohexyl (Acetohexamide), -, 4.0; 4,3-Me(H₂N)C₆H₃, 1-adamantyl, 175° (decomp.), 0; 4,3-Me(H₂N)C₆H₃, cyclohexyl (Metahexamide), -, 5.0; 4-MeC₆H₄, 2-adamantyl, 206-8°, 4.0; 4-MeC₆H₄, 3-methyl-1-adamantyl, 184-6°, 2.8; 4-MeC₆H₄, 3,5-dimethyl-1-adamantyl, 166-8°, 0; 4-EtC₆H₄, 1-adamantylmethyl, 203-5°, 0.2; 4-AcC₆H₄, 1-adamantylmethyl, 204-6°, 0. The pharmacol. evaluation of the compds. is discussed, particularly with respect to IX. Preliminary clinical data thus far indicate IX to be a most satisfactory, potent oral hypoglycemic agent with an effective av. dose, single or divided, of 400 mg./day. IX is equal to Chlorpropamide on a wt. basis and possesses about 5 times the potency of Tolbutamide. The activity of IX is rapid in onset with tentative duration of 4-6 hrs., indicating that IX is rapidly absorbed and utilized by the body.

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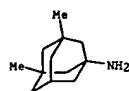
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IT 41100-52-1, 1-Adamantanamine, 3,5-dimethyl-, hydrochloride (preparation of)

RN 41100-52-1 CAPIUS

CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

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